

# Biting Off More Than You Can Chew: The Surprising Relationship Between Periodontal Disease and Diabetes Mellitus

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## ABSTRACT:

Particularly type 2 diabetes (T2DM), periodontitis is often related with chronic inflammatory illness of infectious origin. By releasing pro-inflammatory cytokines including TNF- $\alpha$  and IL-1 $\beta$ , periodontitis aggravates insulin resistance in this reciprocal interaction including inflammatory mechanisms. Conversely, diabetes compromises the immune system and promotes the growth of bacteria, therefore causing periodontal disease. Studies reveal that those with diabetes have about three times higher chance of getting periodontitis. that bad glycemic control worsens periodontal health. Studies on data up to October 2023 reveal a robust relationship between diabetes progression and gum disease severity, emphasizing Systemic markers such IL-6, CRP, and fasting blood affected by periodontal inflammation levels of sugar. Effective periodontal treatment has been related to enhanced glycaemic control, underline the importance of integrated medical and dental treatment. One must grasp this. reciprocal connection to develop targeted therapy strategies meant to reduce one disease while improve overall health outcomes.

**KEYWORDS:** Periodontal disease, Diabetes mellitus, Inflammatory Disease, Inflammatory Mediators, Diabetes Mellitus

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## INTRODUCTION

Periodontitis<sup>1</sup>, A chronic inflammatory illness of infectious origin<sup>1</sup>, Typically caused by unmanaged gingival inflammation that harms the supporting tissues of the tooth, periodontitis is connected to the development of dental microbial biofilm and is defined by the gradual breakdown of the alveolar bone and periodontal ligament induced by proinflammatory cytokines that promote bone resorption<sup>(1)</sup>, such as tumor necrosis factor (TNF- $\alpha$ ) and interleukin 1 beta (IL-1 $\beta$ ).<sup>1</sup>

Patients with diabetes(1), the condition most closely associated with periodontitis(1), are known to be at a heightened risk of acquiring periodontitis(1), particularly when the condition is left untreated.<sup>1</sup>

Based on the results of the oral glucose tolerance test (OGTT)<sup>2</sup>, hemoglobin A1c (HbA1c)<sup>2</sup>, and fasting plasma glucose (FPG)<sup>2</sup>, the American Diabetes Association (ADA) established three diagnostic criteria for the diagnosis of diabetes; nevertheless, there are variations in these assays' sensitivity, variability, and repeatability<sup>2</sup>. According to available data, alterations in the state of periodontal disease could serve as a trustworthy predictor of the occurrence of diabetes.<sup>2</sup>

According to epidemiological research, diabetes is a significant risk factor for developing periodontitis; individuals with diabetes are almost three times more likely to develop periodontitis.<sup>3</sup>

Although the exact mechanisms behind the connections between these two disorders are unknown, they include elements of neutrophil activity, cytokine biology, and immunological functioning.<sup>3</sup>

There is growing evidence that diabetes and periodontitis are related in both directions, with diabetes raising the chance of developing periodontitis and periodontal inflammation impairing glycaemic management<sup>3</sup>

Although type 1 diabetes mellitus is known to be a risk factor for periodontitis, the majority of research focuses on type 2 diabetes mellitus (T2DM) as a risk factor<sup>1</sup>

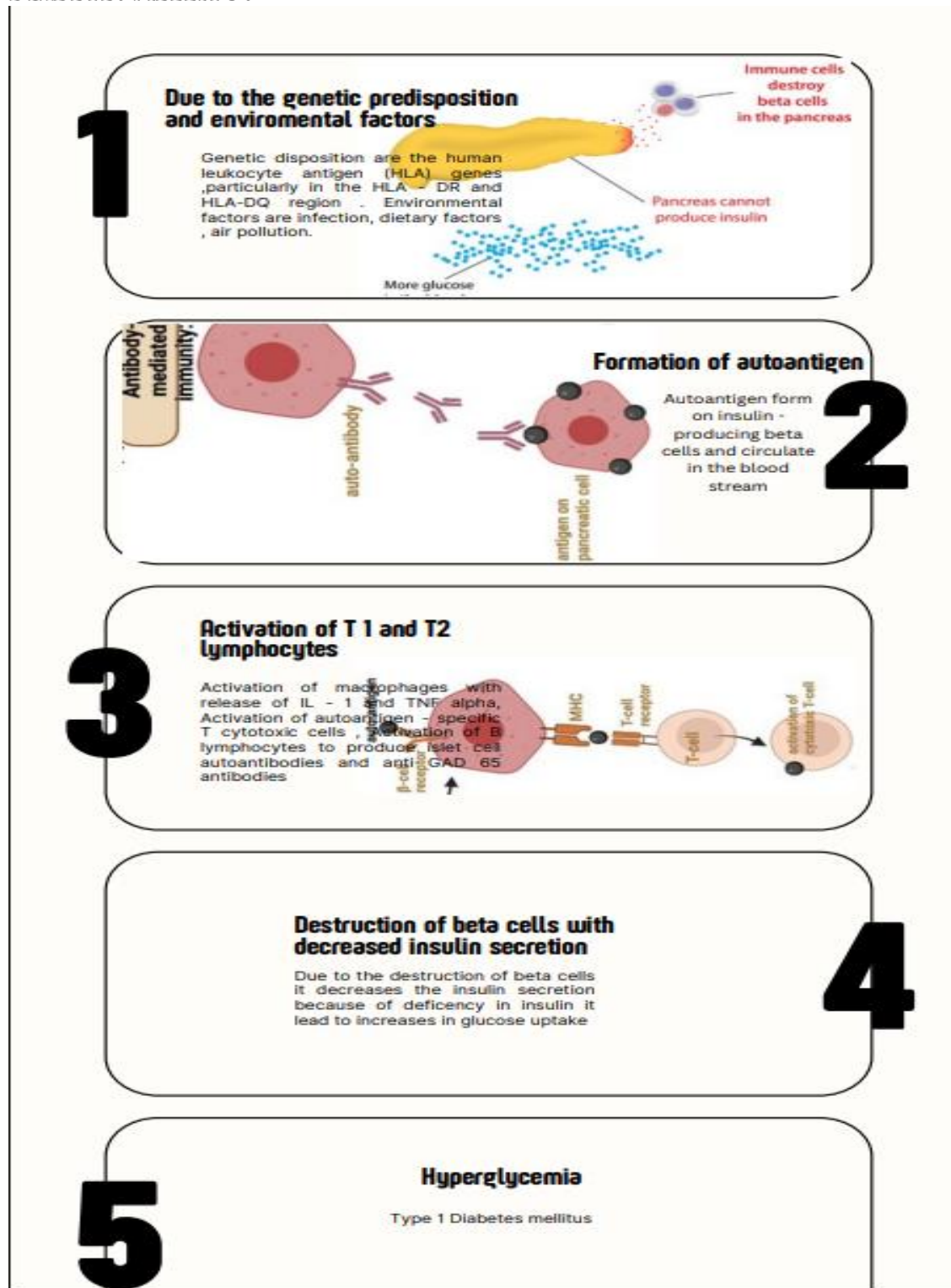
HbA1c decreases of roughly 0.4% are linked to periodontitis treatment. It is important to promote oral and periodontal health as essential elements of managing diabetes<sup>4</sup>

These kinds of studies are crucial because they can provide light on the temporal relationship between type 2 diabetes and periodontal disease.

The connections with diabetes We postulated that incident type 2 diabetes in the First National Health and Nutrition Examination Survey (NHANESI) and its Epidemiologic Follow-up Study (NHEFS) was predicted by baseline periodontal disease<sup>5</sup>

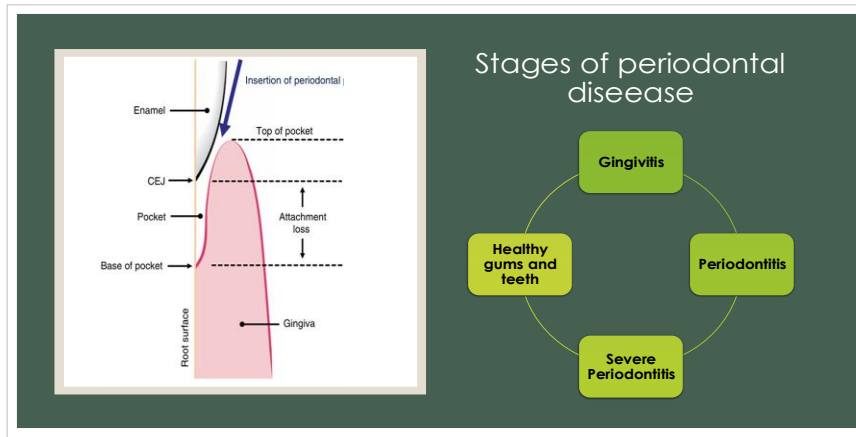
Multiple missing teeth from PD or other reasons are common in diabetic individuals. Consequently, utilizing dental implants to replace these patients' lost teeth is one of the most popular therapy regimens<sup>3</sup>. However, there is evidence that people with diabetes should be treated carefully when choosing implant therapy since they are more likely to experience problems such as peri-implant disease.<sup>3</sup>

### DIABETES MELLITUS (7,12,13)



### PERIODONTITIS

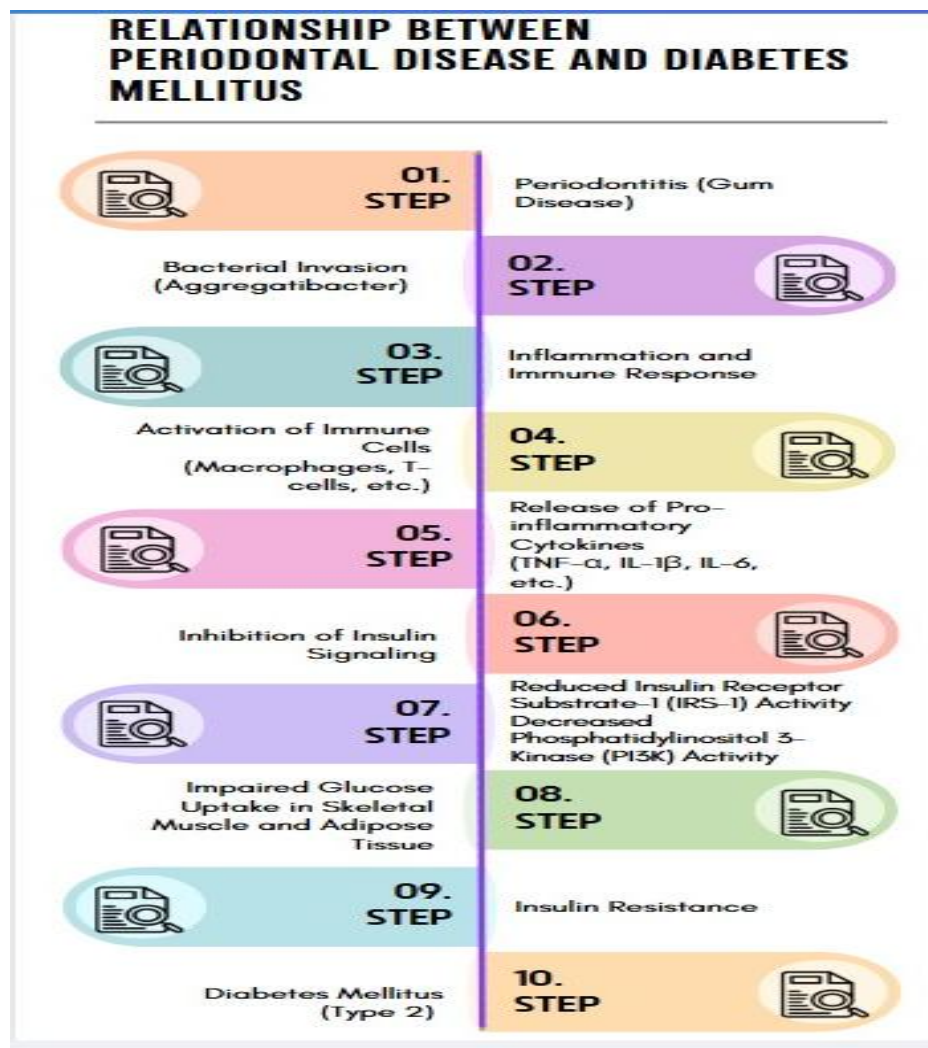
A periodontal pocket forms between the gingiva and the tooth as a result of tissue deterioration in periodontitis<sup>3</sup>, which breaks down the collagen fibers of the periodontal ligament<sup>14,4</sup>. In terms of mechanism, infections typically result in gingival sores and tissue contamination around the teeth.<sup>3</sup>



Once the bacterial infection and the inflammatory response target the root surface and penetrate the tooth's supporting components, the lesion develops into periodontitis.<sup>4</sup> Generally speaking, phagocytes (macrophages and neutrophils) that migrate to the lesion site start the inflammatory process and become inflamed.<sup>3</sup> The inflammation in periodontal is called periodontitis.<sup>3,14,4</sup>

### DIABETES MELLITUS CAUSED BY PERIODONTAL DISEASE

Investigations into members of the Gila River Indian community provided the first convincing proof in favor of this theory.<sup>8</sup> A higher likelihood of poor glycaemic control (HbA1c > 9.0%) during follow-up (at least two years) was linked to severe periodontitis at baseline, indicating that severe periodontitis was a risk factor for inadequate diabetes treatment.<sup>8</sup> Furthermore, some studies have shown a correlation between the severity of periodontitis and the prevalence and severity of non-oral diabetes-related problems, such as retinopathy, diabetic neuropathy, proteinuria, and cardiovascular issues.<sup>8</sup>



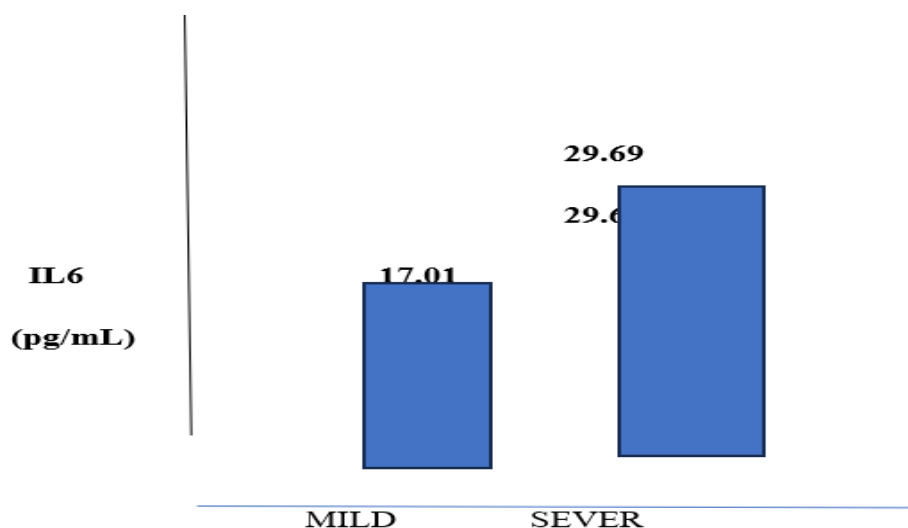
It is now widely acknowledged that periodontitis, a chronic inflammatory gum disease brought on by bacterial pathogens like *Aggregatibacter actinomycetemcomitans*, is a major risk factor for systemic diseases like Type 2 Diabetes Mellitus (T2DM).<sup>8</sup> An series of inflammatory and metabolic series Abnormalities are part of the pathologic link between periodontitis and type 2 diabetes The disease begins when bacteria enter periodontal tissues, triggering a local immune reaction. that releases pro-inflammatory cytokines such interleukin-1 beta (IL-1 $\beta$ ), interleukin-6 (IL-6), and TNF- $\alpha$ : tumor necrosis factor-alpha.<sup>8</sup> Once these cytokines get into the circulation, they increase inflammatory markers all over the body and stimulate immune cells like T-cells and macrophages, which even more strengthens inflammatory signals.<sup>8</sup>

Development of insulin resistance depends on a key process: prolonged exposure to these inflammatory mediators<sup>9</sup> acting on insulin signalling pathways Particularly, TNF- $\alpha$  and IL-1 $\beta$  impede insulin receptor substrate-1 (IRS-1) activity, therefore reducing Phosphatidylinositol 3-kinase (PI3K) is activated.<sup>9</sup> Because PI3K is essential for the translocation of glucose transporter-4 (GLUT-4), its deficiency causes skeletal muscle and adipose tissue to absorb glucose less efficiently.<sup>9</sup> This inflammation that keeps happening turns finally makes insulin resistance—characteristic of type 2 diabetes—worsens.<sup>9</sup> Furthermore, oxidative stress and Endothelial dysfunction induced by periodontitis could aggravate metabolic dysregulation. - producing a terrible loop linking periodontal disease and diabetes.<sup>9</sup>

Recent studies strengthen the bilateral relationship between periodontitis and diabetes by suggesting that treating the former can enable diabetic patients to reach improved glycemic control.<sup>11</sup> Understanding this molecular pathway highlights the need of coordinated dental and medical treatment for Managing and avoiding type 2 diabetes.<sup>11</sup> To break this pathogenic link and provide new approaches to diabetes management and prevention, future research should investigate targeted anti-inflammatory therapies.<sup>11</sup> Eighty persons with gum inflammation took part in this research; forty had mild gum and the other forty displayed serious gum inflammation.<sup>8</sup>

#### **A comparison of IL 6 levels for mild and severe gum inflammation<sup>8</sup>**

Diabetes was also identified in each subject. The results showed significant differences ( $P \leq 0.01$ ) in IL-6 between the mild and severe gum inflammation.<sup>8</sup>

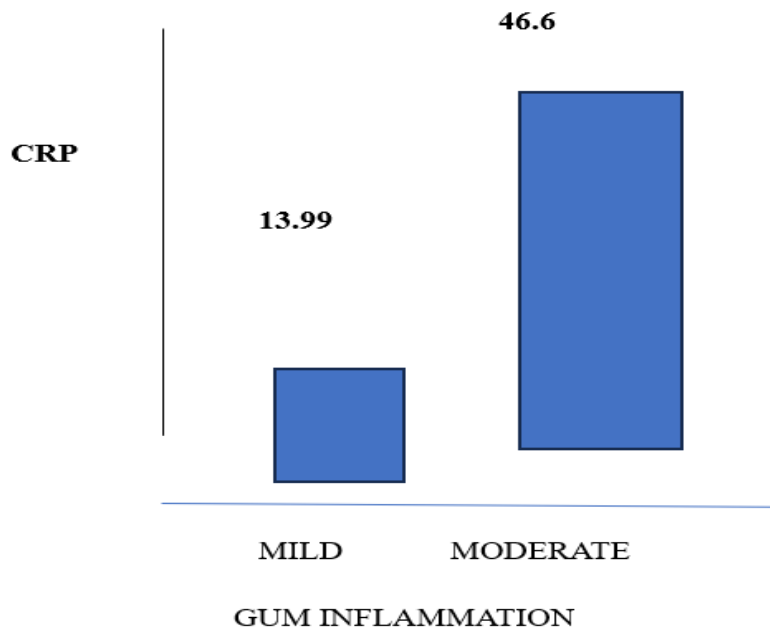


Gum inflammation is linked to the anti-inflammatory cytokine IL-6, which contributes to the understanding of oral inflammation<sup>8</sup>

Gum disease is brought on by germs on the gums and teeth, as well as an inflammatory and immunological reaction<sup>8</sup> Gingivitis-induced inflammation raises interleukin-6<sup>8</sup> IL-6 fights bacteria and controls inflammation; it is said that too high IL-6 levels might make tissue and gum inflammation worse.<sup>8</sup> There is broad evidence that increased IL-6 levels are the cause of gum inflammation<sup>8</sup>

#### **A comparison of CRP levels for mild and severe gum inflammation<sup>8</sup>**

A study of CRP (C-reactive protein) levels for mild and severe gum inflammation showed that there were significantly more differences ( $P \leq 0.01$ ) between the groups with severe and moderate gum inflammation.<sup>8</sup>

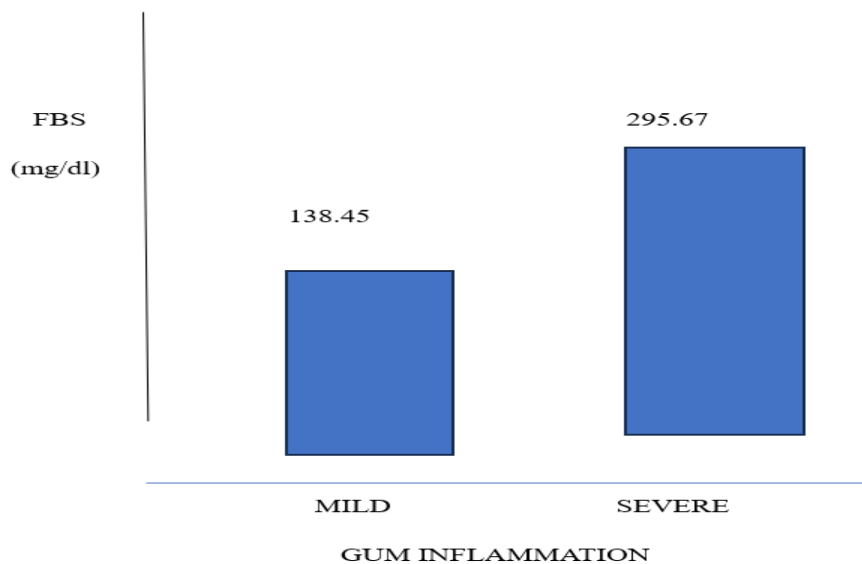


The liver produces CRP in reaction to inflammation, which frequently signifies systemic inflammation<sup>(8)</sup>. According to Pejic et al. (2011), gum inflammation is measured by C-reactive protein. The incredibly notable differences between severe and moderate CRP levels<sup>8</sup>

Gum inflammation groups demonstrate that a more robust systemic inflammatory response is triggered by severe gum inflammation.<sup>8</sup> One explanation is that excessive gum inflammation causes the blood to contain more inflammatory mediators, such as CRP.<sup>8</sup>

FBS levels for mild and severe gum inflammation are compared.<sup>8</sup>

The results demonstrated that the groups with moderate and severe gum inflammation had statistically significant differences ( $P \leq 0.01$ ) in their fasting blood sugar levels.<sup>8</sup>



Chronic inflammation, such as that found in severe gum inflammation, has been shown to disrupt glucose metabolism, causing an imbalance in blood sugar levels that may lead to high fasting blood glucose levels.<sup>8</sup>

Poor glucose metabolism and high fasting blood glucose are symptoms of type 2 diabetes.<sup>8</sup> Diabetes may worsen or be brought on by gum inflammation, which raises the body's inflammatory load.<sup>8</sup>

Notable are the findings demonstrating statistically significant differences ( $P \leq 0.01$ ) in fasting blood sugar levels between the groups with moderate and severe gum inflammation.<sup>8</sup>

## RISK OF PERIODONTAL DISEASE BY DIABETES MELLITUS<sup>8,10</sup>

Because diabetes raises blood glucose levels, it can encourage the growth of oral bacteria.<sup>8</sup> This could increase the risk of gum disease. Diabetes impairs immunity, making it more difficult to prevent gum infections.<sup>8</sup>

Diabetes can exacerbate or prolong inflammation, increasing the risk of periodontitis and gingivitis, or inflammation of the gums.<sup>10</sup>

The relationships and importance of periodontal index (PI) in individuals with diabetes.<sup>10</sup> Only age, the length of known diabetes, blood sugar level variance, and the existence of complications were significant when the individual contributing factors were examined for effects on PI independent of the other variables.<sup>10</sup>

The probability value was less than 0.05 for the relationships between PI and the other three variables and less than 0.01 for the relationship between PI and age.<sup>8</sup> Age, the length of known diabetes, and the existence of complications were all substantially correlated with the number of teeth lost as a result of periodontal disease.<sup>8</sup>



Through several interrelated pathways, uncontrolled diabetes mellitus, which is typified by chronic hyperglycemia, significantly contributes to the etiology and development of periodontal and peri-implant disorders.<sup>8</sup> Advanced glycation end products (AGEs) build up as a result of chronic hyperglycemia. These AGEs attach to their receptors (RAGE) on periodontal tissues, causing oxidative stress and an excess of reactive oxygen species (ROS).<sup>8</sup> Cellular healing systems are hampered, and tissue damage is made worse by an oxidative environment.<sup>8</sup>

Hyperglycemia also encourages a pro-inflammatory state<sup>10</sup>, which is characterized by higher levels of cytokines like interleukin-6 (IL-6), interleukin-17 (IL-17), and tumor necrosis factor-alpha (TNF- $\alpha$ ).<sup>10</sup> These inflammatory mediators decrease the host's capacity to fight off bacterial infections by impairing

neutrophil function and continuing the deterioration of periodontal tissue.<sup>10</sup> The immunological dysfunction that results makes it easier for harmful bacteria to proliferate<sup>10</sup>, which speeds up the advancement of periodontal disease and makes people more vulnerable to peri-implant infections.<sup>10</sup> Additionally, microvascular difficulties brought on by diabetes reduce blood supply to periodontal tissues, which hinders wound healing and raises the risk of infection.<sup>8</sup> Because diabetes and periodontal disease are inversely correlated, poorly managed diabetes deteriorates periodontal health, and severe periodontitis further impairs glycemic control, resulting in a vicious cycle.<sup>8</sup>

## DISCUSSION

The most recent systematic review, which compiled observational studies examining the reciprocal link between diabetes and periodontal disease, deviated from our findings by showing that severe periodontitis raised the risk of type 2 diabetes by 53%.<sup>9</sup>

An earlier meta-analysis and systematic review that included six studies from 2013 to 2017—the majority of which were carried out in Taiwan and Japan—also found that people with periodontal disease were more likely to develop diabetes than people without the condition.<sup>9</sup>

Lastly, there is a complex interaction between gum inflammation, IL-6, CRP, and fasting blood sugar.<sup>8</sup> CRP, IL-6, and fasting glucose are all impacted by GUM inflammation. IL-6 stimulates the immune system in cases of severe gum inflammation.<sup>8</sup>

CRP rises with severe gum inflammation, indicating a systemic inflammatory environment that may impact CHD and other illnesses.<sup>8</sup> Severe and moderate gum inflammation changes glucose metabolism because of changes in fasting blood sugar.<sup>8</sup> According to this study, severe gum disease that changes insulin sensitivity may increase the risk of diabetes and fasting blood sugar.<sup>8</sup>

## CONCLUSION

The idea that DM can have detrimental consequences on people is supported by the clinical and epidemiological data in the literature we evaluated.<sup>11</sup> PD is linked to a higher risk of complications from diabetes.<sup>11</sup>

However, to prove these associations and that treating Periodontal disease can improve glycaemic control and potentially lessen the burden of complications related to diabetes.<sup>11</sup>

Treatment for diabetes mellitus and periodontal disease both enhance clinical results.<sup>8</sup>

Periodontal disease and diabetes mellitus have a bidirectional relationship because DM can increase AGE, ROS, inflammation (TNF – IL6, IL 17), and impaired neutrophil function that may lead to periodontal disease, and PD can cause insulin resistance by invasion of bacteria that may lead to DM.<sup>8</sup>

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