

# The Relationship between Diabetes Mellitus and Periodontal Disease

Arni I. Djais

Department of Periodontics Faculty of Dentistry, Hasanuddin University, Makassar, Indonesia

Corresponding Author: irawatyarni1975@gmail.com

DOI: 10.47750/pnr.2023.14.02.315

## Abstract

**Objective:** The aims to elucidate the major complications of diabetes, the increased risk and severity of periodontitis and to provide a basic mechanism for the association of diabetes mellitus with periodontal disease.

**Materials and Methods:** An initial search was conducted of the PubMed, Elsevier and Science Direct databases Online to evaluate articles on the relationship of diabetes mellitus to periodontal disease. The initial result of this search was 4037 articles. Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) by using the system Population/Problem, Intervention, Comparison/Control, and Outcome (PICO). After manual selection, only 5 articles will be synthesized.

**Results:** From these five articles it was found that Diabetes mellitus can increase the risk of severity and prevalence of periodontal disease caused by an increase in inflammatory cells in the periodontal tissue.

**Conclusion:** Diabetes can increase the risk of the severity and prevalence of periodontal disease.

**Keywords:** Diabetes mellitus, Periodontal disease, Periodontitis

## INTRODUCTION

The International Diabetes Federation (IDF) in 2019 estimated that at least 463 million people aged 20-79 years or around 9.3% of the world's total population suffer from diabetes.<sup>1,2</sup> Diabetes mellitus (DM) is defined as a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both.<sup>2</sup> In general, diabetes mellitus is divided into 3 main types namely, diabetes mellitus type 1 (DMT1), diabetes mellitus type 2 (DMT2), gestational diabetes mellitus (GDM).<sup>3</sup> Diabetes Mellitus is one of the risk factors for periodontitis, which results in a threefold increased susceptibility to periodontitis. Research conducted by Hong M, et al in 2017 in Korea showed that the prevalence of periodontal disease in patients with diabetes mellitus increased by 18.7% compared to normoglycemic patients.<sup>(4)</sup> A similar study was also conducted by Su N, et al in 2020 in Amsterdam, the Netherlands showing that bone loss was >50% in patients with diabetes mellitus with a prevalence of 21.9% higher than normoglycemic patients which was only 12.5%.<sup>5</sup> Some of these studies prove that diabetes mellitus can increase the inflammatory response and tissue damage. This is because diabetes mellitus is often associated with host metabolic dysregulation which can increase the occurrence of periodontal inflammation and poor glycemic control.<sup>6</sup> The purpose of this literature review is to describe the major complications of diabetes, the increased risk and severity of periodontitis and to explain the pathomechanism of the association of diabetes mellitus with periodontal disease.

Periodontitis is defined as an inflammatory disease of the supporting tissues of the teeth caused by microorganisms resulting in destruction of the periodontal ligament and alveolar bone with increased pocket formation, bleeding on probing, recession, or both.

The clinical feature of periodontitis is the presence of clinically detectable attachment loss as a result of inflammatory damage to the periodontal ligament and alveolar bone. This attachment loss is often accompanied by the formation of periodontal pockets and changes in the density and height of the underlying alveolar bone. Clinical signs of inflammation such as changes in color, contour, and consistency and bleeding on probing are not always positive indicators of clinical attachment loss. However, if there is continued bleeding after probing, it is an indicator of inflammation and an increased risk for clinical attachment loss. There are three main types of periodontitis, namely

chronic periodontitis, Chronic periodontitis is an inflammation due to the accumulation of plaque and calculus which has a fairly slow disease progression. The increase in the rate of disease progression is caused by the impact of local, systemic, or environmental factors that can influence the host-bacteria interaction. Aggressive periodontitis is an inflammatory disease that progresses very quickly and is usually seen in healthy individuals without the accumulation of plaque and calculus. It is usually associated with a family history and is suggestive of a genetic trait. Periodontitis as a manifestation of systemic disease is influenced by the effects of systemic disorders through changes in the immune response.

The mechanism of periodontitis is induced by pathogenic biofilm or dental plaque, which accumulates on the tooth surface namely the 'Red complex' Gram-negative bacteria, consisting of *Porphyromonas gingivalis*, *Tannerella forsythia* and *Treponema denticola*. These bacteria can trigger changes in the number and composition of oral commensal microbiota that can disrupt homeostasis and cause inflammatory periodontal bone loss. Inflammation in periodontitis is characterized by leukocyte infiltration, which limits the level of bacterial invasion and can be harmful to the periodontal tissue and then destruction of bone and periodontal ligament is thought to be caused by a disruption of the homeostatic balance between the host and bacterial responses, which causes inflammation. This process is one of the involvements between the host immune response to bacterial infection through the stimulation of osteoclastogenic factor production by immune cells, which then helps to cause bone loss associated with periodontitis. Thus, periodontitis is a complex disease and has many risk factors. Risk factors include the individual's genetic and immune inflammatory status, and the presence of environmental factors or systemic disease, such as diabetes.

Diabetes mellitus is a chronic condition resulting from elevated levels of glucose in the blood because the body cannot produce enough insulin or use insulin effectively. Lack of insulin or the inability of cells to respond to insulin leads to increased blood glucose levels or hyperglycemia. Hyperglycemia that is left for a long time can cause organ dysfunction. In general, diabetes is divided into 3 main types, namely diabetes mellitus type 1 (DMT1), diabetes mellitus type 2 (DMT2) and gestational diabetes mellitus (GDM).

Diabetes mellitus type 1 (DMT1) is an autoimmune reaction due to the body's immune system attacking insulin-producing beta cells in the pancreas gland. As a result, the body does not produce insulin until a relative or absolute insulin deficiency occurs. Signs and symptoms of DMT1 include: polydipsia, polyuria, polyphagia, dry mouth, lack of energy, fatigue, significant weight loss, bad wetting, and blurred vision.

Diabetes mellitus type 2 (DMT2) is a multifactorial disease that causes hyperglycemia due to inadequate insulin production and the body's inability to fully respond to insulin. Important risk factors that may contribute to DMT2 include: excess adiposity (obesity), poor diet and nutrition, unhealthy physical activity, prediabetes or impaired glucose tolerance (IGT), smoking and a history of GDM with exposure of the unborn child to high levels of glucose. high during pregnancy. Signs and symptoms of DMT2 include: polydipsia, polyuria, polyphagia, dry mouth, lack of energy, fatigue, frequent tingling/numbness in the hands and feet, recurrent fungal infections of the skin, slow wound healing and blurred vision.

Gestational diabetes mellitus (GDM) is an increase in blood glucose levels / hyperglycemia that occurs during pregnancy. GDM arises because reduced insulin function (insulin resistance) due to hormone production by the placenta. Other risk factors for GDM include older age, being overweight or obese, excessive weight gain during pregnancy, a family history of diabetes and a history of delivering a baby with a congenital abnormality. GDM usually exists as a temporary disorder during pregnancy and resolves after the pregnancy ends.

Diabetes is a predisposing factor for periodontitis, and periodontitis is a poor glycemic factor. The relationship between diabetes and periodontitis is explained by several mechanisms: (1) microvascular changes, (2) gingival crevicular fluid changes, (3) collagen metabolism disorders, (4) changes in host immune response, (5) subgingival fluid changes, (6) genetic predisposition. and (7) enzymatic glycation.

Oral manifestations found in diabetic patients consist of cheilosis, dry mouth, burning mouth, less salivary flow and changes in the oral microflora which are dominated by *Candida albicans* and gram-positive bacteria. Diabetic patients had more proinflammatory cytokines in the gingival fluid than

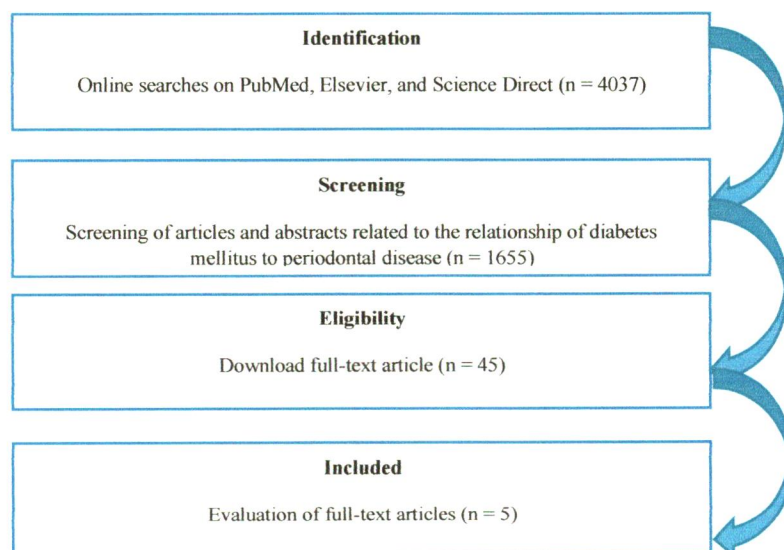
non-diabetics, at the same severity of periodontitis. The impaired adhesion found in diabetics is caused by the downregulation of Intracellular Adhesion Molecule 1 (ICAM-1) in the vessel wall during inflammation. In addition, Advanced Glycosylation End Product (AGE) formed during hyperglycemia alters the formation of the formyl-Met-Leu-Phe peptide, a PMN chemotactic regulator. The interaction between leukocytes and endothelial cells is also inhibited by the sorbitol and polyol pathways of activation during hyperglycemia.

In diabetic patients, monocytes and PMNs are hyper-responsive to lipopolysaccharide (LPS) exposure, leading to the release of cytokines. AGEs also play a role in this hyper-reactivity by binding to monocyte receptors and activating Nuclear Factor Kappa B (NF- $\kappa$ B), which alters the transcription of pro-inflammatory cytokine genes. These pro-inflammatory cytokines continuously circulate in the systemic circulation and cause tissue destruction in the periodontium.

## Material and Methods

The method used is Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA)<sup>14</sup> by using the system Population/Problem, Intervention, Comparison/Control, and Outcome (PICO).<sup>15</sup> Initial searches were carried out from the PubMed, Elsevier and Science Direct databases on the association between diabetes mellitus and periodontal disease. The keywords used were “Diabetes Mellitus”, “Periodontal Disease” The initial results of this search were 4037 articles. After manual selection, only 5 that have been defined as articles will be synthesized. The article is an article from Hong et al (2017), Bazyar H, et al (2019), Lee CH, et al (2019), Battancs E, et al (2020) and Su N, et al (2020).

The inclusion criteria in this writing are scientifically published articles that are available online, published in the last 5 years (2016-2021), articles related to diabetes mellitus and periodontal disease, articles that examine the relationship between diabetes mellitus and periodontal disease, articles related to diabetes mellitus and periodontal disease. has complete data or does not only present abstracts and not articles with the type of research Literature review and Systematic Review. At this writing, the author chooses articles independently to find articles that meet the inclusion criteria. Each article is carefully selected by filtering title, abstract, method and results. After that, the author makes a list of the final synthesis that will be used in this paper.



**Figure1.** PRISMA Flow Chart

Table 1. Journal analysis table

DISCUSSION

No	Author//Year	Research type and design	Sample	Sample Criteria	Results
1.	Hong M, et al (2016) Prevalence and risk factors of periodontitis among adults with or without diabetes mellitus	Descriptive Research	4,477 people with DM	Fasting plasma glucose 126 mg/dL CPI value: 3 or 4 Pocket Value: 3.5 mm	The prevalence of the periodontitis group with DM was 18.7%, which was significantly higher than the non-periodontitis group only (9.0%, $p < 0.001$ ). The prevalence of periodontitis adjusted for sample values in the Korean population was 43.7% in the DM group and 25% in the non-DM group ( $p < 0.001$ )
2.	Bazyar H, et al (2019) The relationship between metabolic factors and anthropometric indices with periodontal status in diabetes mellitus type 2 patients with chronic periodontitis	Descriptive Research	100 people with DM and 100 healthy people as control group	Age 30-60 years, there are at least 20 teeth in it, without any other systemic disease	Periodontal indices including BOP, CAL, PD and plaque index were also significantly higher in patients with diabetes ( $p < 0.001$ )
3.	Lee CH, et al (2019) Correlation between diabetes mellitus and periodontitis in Taiwan: A nationwide cohort study	Descriptive Research	39,384 patients with DM	DM patients aged > 20 years without periodontitis before DM (2005 - 2012)	Based on the results of calculations using Adjusted Hazard Ratios (aHR) for periodontitis between patients with and without DM. showed that patients with DM had a higher risk with a score of 1.04 (95% CI: 1.01-1.08) than patients without DM.
4.	Battancs E, et al (2020) Periodontal Disease in Diabetes Mellitus: A Case- Control Study in Smokers and Non-Smokers	Descriptive Research	32 people with DM without smoking habits (NSDM) Then the control group, namely 32 people without smoking habits and no DM (NSC)	BMI < 30 kg/m <sup>2</sup> , tooth loss < 2, OHIS value < 3	Based on the results of the assessment, it was found that, from 32 people the prevalence of NSDM had severe periodontal disease 28%, moderate 59%, mild 6%. For the control group of 32 NSC, the prevalence of periodontal disease was severe 16%, moderate 37%, mild 34%
5.	Su N, et al (2020) Development and validation of a screening model for diabetes mellitus in patients with periodontitis in dental settings	Descriptive Research	204 patients with periodontitis	Patients with periodontitis, patients aged > 18 years	Based on the results of the study, it was found that the prevalence of patients with severe periodontitis in DM patients was 51.4% compared to non-DM patients, which was only about 31%.

Several studies that discuss the relationship between diabetes mellitus and periodontal disease, such as that conducted by Hong et al,<sup>4</sup> conducted research using data from KNHANES or the Korean national dental health agency. A total of 4,477 samples of individuals aged 30 years with DM were evaluated. Based on the grouping results, it was found that the prevalence of the periodontitis group with DM

was 18.7%, which was significantly higher than the non-periodontitis group which was only (9.0%,  $p < 0.001$ ). The prevalence of periodontitis adjusted for sample values in the Korean population was 43.7% in the DM group and 25% in the non-DM group ( $p < 0.001$ ). This proves that diabetes can increase periodontal tissue damage due to hyperglycemia so that it produces advanced glycation end product, causes macrophage activation, increases inflammatory cytokines and reactive oxygen species which increases the destruction of the periodontal tissues. Bazyar H et al,<sup>16</sup> conducted a study using a case group consisting of 100 patients with T2DM and periodontal disease and a control group consisting of 100 healthy subjects. The data found that an increase in periodontal indices including BOP, CAL, PD and plaque index was also significantly higher in patients with diabetes ( $p < 0.001$ ). This is because inflammatory mediators, especially IL-6 and TNF-, which are released from the periodontal tissues in response to bacteria and inflammation, enter the bloodstream and ultimately reduce insulin sensitivity by binding to insulin receptors. Lee CH et al,<sup>17</sup> conducted a study using the NHIRD database with a case group consisting of 39,384 patients with DM. Based on the results of calculations using Adjusted Hazard Ratios (aHR) for periodontitis between patients with and without DM, it shows that patients with DM have a higher risk with a value of 1.04 (95% CI: 1.01-1.08) than patients without DM. So this study shows that patients with DM have a higher risk of periodontitis than patients without DM based on the NHIRD database. In patients with DM, the concentration of oral microbial flora is increased due to higher glucose concentrations in saliva and crevicular fluid. Persistent hyperglycemia leading to an immune-inflammatory response to periodontal pathogens, Battancs E et al, conducted a study using a database from the Department of Internal Medicine, Hungary's Szaged University with 64 samples consisting of 32 samples with the Non-smoking patient with Diabetes Mellitus (NSDM) group and 32 samples with the Non-Smoking without Diabetes Mellitus (NSC) group. ). The data from this study were obtained from 32 people showing the prevalence of periodontal disease (PD) in Non-smoking patients with Diabetes Mellitus (NSDM) of 28% severe PD, 59% moderate PD, 6% early PD while for the control group of 32 non-smokers. -Smoking without Diabetes Mellitus (NSC), has a prevalence of severe PD 16%, moderate PD 37%, early PD 34%. This is because DM can reduce the antibacterial capacity of saliva so that it supports the growth of periodontopathogenic bacterial species. The end result is an increase in inflammatory cells in the periodontal tissues. This can be exacerbated by patients who have a habit of smoking, because smoking can accelerate the effects of damage to the periodontal tissues and maintain a high level of inflammation severity through repeated exposure to the tissue. Su N et al,<sup>5</sup> conducted a study using a database of 204 samples from the periodontology department at the Academic Center of Dentistry Amsterdam (ACTA). In the results of this study. it was found that the prevalence of patients with severe periodontitis in DM patients was 51.4% compared to 31% in non-DM patients. Based on several studies that have been described, there are several similarities, namely Diabetes mellitus can increase the risk of the severity of periodontal disease caused by an increase in inflammatory cells in the periodontal tissue. Some of the differences in the results obtained are influenced by certain factors such as age, different glucose levels, and bad habits etc. owned by the patient. These factors can increase the severity of periodontal disease and cause differences in the values obtained by the researchers.

## CONCLUSION

Diabetes Mellitus has a close relationship with an increase in the prevalence and risk of severity in periodontal disease, this is because hyperglycemia in people with diabetes mellitus can increase inflammatory cells in the periodontal tissue.

## Acknowledgment

The author would like to thanks to Faculty of Dentistry, Hasanuddin University, Makassar for support in processing the article.

## Conflict of Interest

The authors report no conflict of interest.

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