International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2025: 7.089

The Nexus of Excess Sugar Intake, Diabetes Mellitus and Periodontitis - A Review

Dr. Muskan[1], Dr. Vikas Jindal[2], Dr. Abhinav Bhasker[3], Dr. Shiva Chauhan[4], Dr. Monika Kumari[5]

Abstract: ***Excessive sugar consumption has emerged as a significant public health concern due to its role in metabolic disorders, particularly diabetes mellitus, and its impact on periodontal health. Excess sugar consumption contributes to obesity, insulin resistance, and chronic hyperglycemia, increasing susceptibility to periodontal inflammation. Conversely, periodontitis exacerbates systemic inflammation, negatively affecting glycemic control and increasing diabetes-related complications. This review explores the intricate relationship between excessive sugar intake, diabetes mellitus, and periodontitis, emphasizing the bidirectional link between diabetes and periodontal disease. It also elaborates on the pathophysiological mechanisms, including impaired immune responses, altered collagen metabolism, and the role of advanced glycation end products (AGEs) in periodontal disease progression among diabetic individuals.***

Keywords: Diabetes Mellitus, Periodontitis, Advanced Glycation End Products, Glycemic Control, Sugar

1. Introduction

Sugar, a ubiquitous component in our daily dietary plan, profoundly impacts our nutrition and health. From the satisfying sweetness in fruits to the hidden sugars in processed foods, sugar's presence in our daily intake is undeniable. To understand its role, it's essential to explore the types of sugar and their effects on our bodies daily.

Natural sugars occur inherently in plant-based foods, including fruits, vegetables, and dairy products.

For example, fruits contain fructose, while milk contains lactose. Vital nutrients, including vitamins, minerals, Fiber, and antioxidants accompany these natural sugars. The Fiber in fruits, for example, prevents rapid spikes in blood glucose levels and provides sustained energy.[1]

Conversely, sugars are incorporated into foods during food processing or preparation. These are regular sugar added to tea and coffees, Corn syrup (explicitly referring to the high-fructose variety) found in canned beverages and packaged foods, and honey. Added sugars, unlike natural ones, have no essential nutrients and are considered "empty calories." You can find them in many products like sugary drinks, baked goods, sauces, and condiments.[2]

The Industrial Revolution improved sugar production, making it a domestic good. Today, sugar is widespread in ultra-processed foods and beverages, enhancing taste and shelf life.

In America, people consume 17 teaspoons, equivalent to 68 grams of sugar, per day, while India, the leading consumer of sugar globally, sees an average person consuming 18 kilograms per annum.[3]

The American Heart Association (AHA) recommends that men consume less than 36 grams of sugar daily and women less than 25 grams daily. Simultaneously, the World Health Organization (WHO) recommends that free sugar intake make up less than 10% of daily calorie consumption.[4]

Maintaining a balanced and healthy diet requires mindful sugar consumption. The World Health Organization (WHO) advises that added sugars (free sugars) should account for less than 10% of the total daily energy intake. Furthermore, reducing sugar intake to below 5% (approximately 25 grams or six teaspoons per day for an average adult) may offer additional health benefits, including a lower risk of obesity and tooth decay.

Individuals consume 2,000 calories a day, equivalent to 200 calories from added sugars, roughly estimated to be 12 tablespoons or 50 grams.[5]

The WHO's 2022 report highlights Southeast Asia's high sugar consumption as a leading factor. Excessive sugar, tobacco, and alcohol use are other key modifiable risks. The 6×6 approach proposes integrating oral diseases with six non-communicable diseases and six risk factors, including sugar and an unhealthy lifestyle. Severe periodontitis, affecting 19% globally in 2019, underscores the importance of addressing lifestyle choices to improve both oral and overall health.[6]

When consumed, sugar is broken down into glucose, i.e., the primary fuel for our body's cells. This glucose is absorbed into the bloodstream, triggering the release of insulin, a hormone that facilitates glucose uptake by the cells. While this process is crucial for energy production, excessive sugar intake can overwhelm the body's regulatory mechanisms.[7]

Excessive intake of these sugars can result in several serious health problems. Firstly, it can contribute to weight gain and obesity, as these sugars add extra calories without promoting satiation. Secondly, the constant spikes and reduction in blood sugar levels can ultimately make the patient more susceptible to resistance to insulin and Diabetes Mellitus (type-2). Additionally, excessive sugar consumption is also related to heart disease, as it can lead to increased triglyceride levels, inflammation, and high blood pressure.[8] Excessive sugar consumption is also linked to inflammation, an imbalance in gut bacteria, metabolic disorders, and long-term health conditions.[9]

This review aims to strengthen the understanding of the association between excessive sugar consumption and periodontal inflammation, emphasizing its significance in the prevention and management of periodontitis, a global public

health concern. Additionally, it explores the interrelationship between periodontitis and diabetes mellitus.

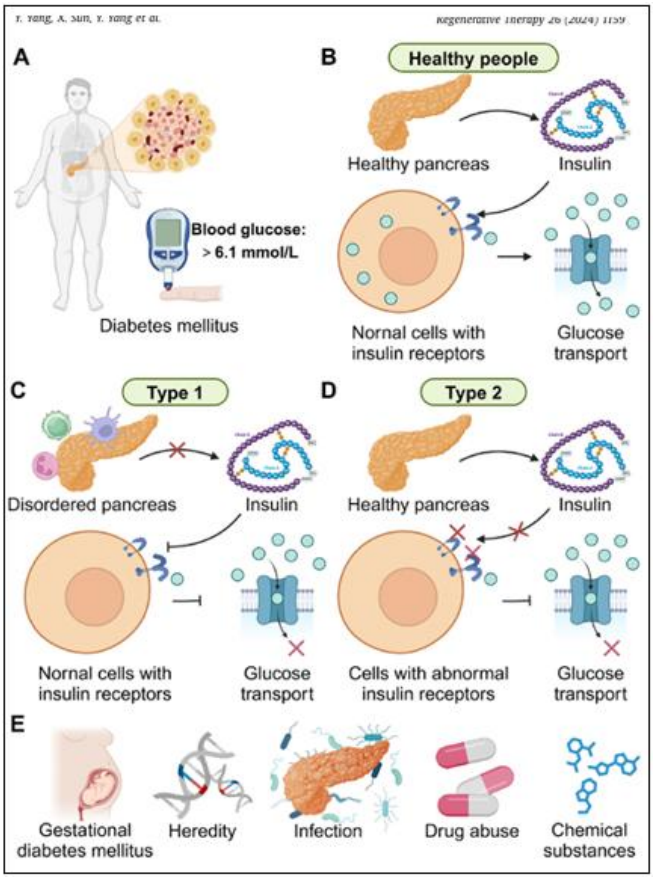

Figure 1: Overview of diabetes mellitus showing normal glucose metabolism, type 1 diabetes, type 2 diabetes, and major etiological factors.

Effects of Diabetes Mellitus on Periodontium:

Diabetes mellitus (DM) comprises a wide range of metabolic disorders, with chronic hyperglycemia being the key characteristic. The etiology of DM involves either the destruction of β-cells, which causes insulin deficiency (type 1 diabetes), or a progressive reduction in β-cell insulin secretion against insulin resistance (type 2 diabetes).[10]International Diabetes Federation (IDF) states that the global DM prevalence reached up to 529 million in 2021, with an age-standardized prevalence of 6.1%, with projections indicating an increase to 1.31 billion by 2050.[11]

Periodontal diseases (PD), affecting the periodontium, are prevalent, impacting 20%-50% of the global population in both developed and developing nations. The Global Burden of Disease Study (2016) ranks severe PD as one of the 11th most prevalent conditions worldwide. The high occurrence of PD in various other groups according to age highlights its importance as a public health concern. Growing evidence suggests a strong link between periodontal diseases and various systemic conditions, including diabetes, cardiovascular disease, and adverse pregnancy outcomes. Both diabetes and periodontal disease are chronic inflammatory conditions that share common risk factors and exacerbate each other, with periodontitis recognized as the sixth complication of diabetes.[12]

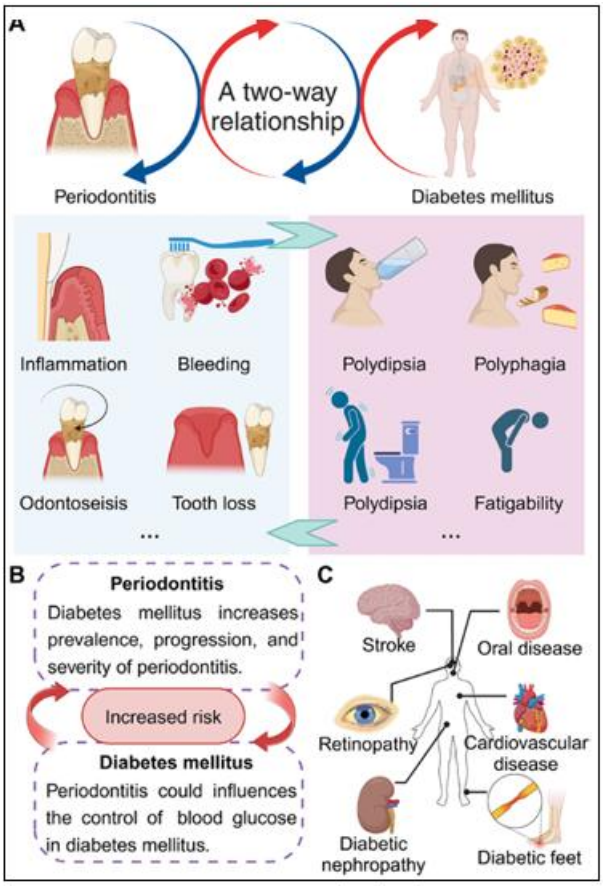

Figure 2: Bidirectional relationship between diabetes mellitus and periodontitis, highlighting mutual influence on disease progression and systemic complications.

The connection between Diabetes mellitus and PD is multifactorial, with significant evidence indicating that diabetes increases susceptibility to periodontal diseases. Conversely, PD can adversely affect glycemic control, creating a vicious cycle between the two conditions. This interplay can be attributed to impaired wound healing, microvascular complications, and an altered host immune response in diabetic individuals. Glycemic control is a critical factor in influencing the severity of periodontal disease in diabetic patients, with well-regulated diabetes contributing to improved periodontal health outcomes.[13]

Despite the recognized association between diabetes and PD, the exact mechanism by which diabetes increases the risk of severe periodontitis remains unclear. However, diabetic individuals exhibit specific pathological alterations. A key issue is the thickening of the basement membrane in small blood vessels, primarily due to the non-enzymatic glycosylation of proteins and the buildup of deposits within the vessel walls and on their inner surfaces. These changes can lead to a narrowing of the blood vessel lumen, potentially impairing nutrient and oxygen transport, which may contribute to periodontal disease progression.[14]

Type I collagen is the main extracellular matrix component present in gingival tissue, the periodontal ligament, and alveolar bone. Metabolic disturbances caused by diabetes mellitus have been linked to disruptions in collagen turnover. Research suggests that gingival and periodontal ligament fibroblasts exhibit impaired metabolism under

hyperglycaemic conditions, leading to reduced cell division and growth, along with heightened collagen activity. Together, these diabetes-related changes in connective tissue metabolism may lead to delayed wound healing and greater severity of periodontal disease.[15]

Dysfunctional polymorphonuclear leukocytes (PMNs), essential for immune defense, have been associated with a heightened risk of periodontal disease. Studies in diabetic individuals have shown impairments in key neutrophil functions, including chemotaxis (movement toward infection sites), adherence, phagocytosis (engulfing bacteria), and bacterial killing. These dysfunctions suggest a weakened host immune response, making diabetic individuals more vulnerable to periodontal infections.[16]

Several factors may contribute to altered neutrophil function in diabetics with periodontitis. One possibility is that periodontal infections themselves may disrupt PMN activity. Additionally, bacterial lipopolysaccharides (LPS) in the infected periodontal tissues can interfere with the neutrophils' oxidative burst—an essential process for destroying harmful bacteria- thereby reducing their ability to eliminate pathogens. Furthermore, systemic lipid levels, particularly unsaturated fatty acids, also influence neutrophil function, potentially exacerbating immune dysfunction in diabetics with periodontitis.[17]

Diabetes-related alterations in the periodontium may be influenced by specific gram-negative bacterial populations. In diabetic patients, the gingival crevicular fluid contains elevated levels of glucose and urea, which can create a favorable environment for changes in the composition of subgingival microbial flora, potentially contributing to periodontal disease progression.[18]

Both type 1 and type 2 diabetes significantly increase an individual's risk of developing severe periodontitis. Evidence from cross-sectional, case-control, and longitudinal studies consistently supports diabetes as a major risk factor for periodontal disease, highlighting the strong association between metabolic dysregulation and periodontal health deterioration.[19]

Păunică I (2023) examines the bidirectional interrelationship between periodontal disease and DM. It highlights how diabetes increases the prevalence, extent, and progression of periodontal disease, while periodontitis adversely affects glycemic control by promoting systemic inflammation and insulin resistance and leading to progression toward diabetes.[20]

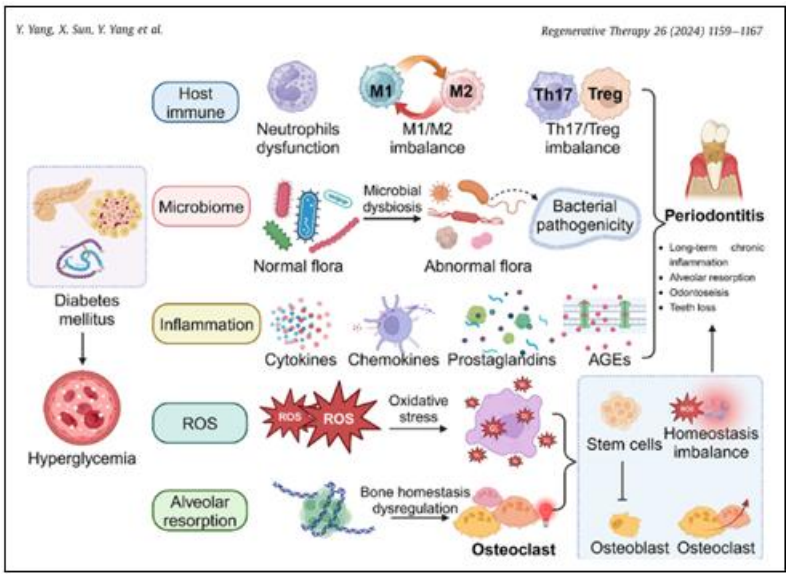

Figure 3: Proposed pathogenic mechanisms linking diabetes mellitus and periodontitis, including hyperglycemia, dysbiosis, immune dysregulation, oxidative stress, AGE formation, and alveolar bone loss.

According to Graves DT (2020), diabetes intensifies inflammatory responses in periodontal tissues, hinders new bone formation, and increases RANKL (Receptor Activator of Nuclear Factor-kB Ligand) expression in response to bacterial challenges. Elevated glucose levels, reactive oxygen species, and advanced glycation end-products in the periodontium of diabetic individuals contribute to heightened activation of nuclear factor-kappa B, leading to the release of inflammatory cytokines such as TNF (Tumour Necrosis Factor) and IL-1(Interleukin-1).[21]

Diabetes disrupts the function of essential immune cells, including neutrophils, monocytes, and macrophages. Neutrophil functions such as adherence, chemotaxis, and phagocytosis are often compromised, diminishing their ability to clear bacteria from the periodontal pocket, which may accelerate periodontal breakdown. While neutrophil function is typically compromised in diabetes, monocytes and macrophages may become hyperactive in response to bacterial antigens. This highlights that the activity leads to an excessive release of proinflammatory mediators and cytokines, further exacerbating inflammation and tissue damage in the periodontium.[22]

A hyperglycaemic state negatively impacts bone health by inhibiting osteoblast proliferation and collagen production, leading to decreased bone formation and weakened mechanical properties of newly formed bone. The impaired balance between cell proliferation, differentiation, and increased cell death contributes to a higher risk of periodontal

attachment loss in diabetic patients. [23] This susceptibility is largely due to deficiencies in connective tissue formation, which fail to keep pace with tissue degradation and remodeling, ultimately compromising the stability of the periodontal attachment apparatus[23]. Elevated plasma glucose levels in diabetic individuals are reflected in increased glucose concentrations within the gingival crevicular fluid. Since the periodontal pocket is a site of ongoing bacterial challenges, an effective wound-healing response is essential for maintaining tissue integrity[24]. However, high glucose levels in the gingival crevicular fluid may directly impair fibroblast function by inhibiting their attachment and spreading- both of which are crucial for wound healing and tissue regeneration- ultimately compromising periodontal repair and maintenance.

In individuals with persistent hyperglycemia, proteins undergo irreversible glycation, leading to the formation of Advanced Glycation End Products (AGEs). These stable, carbohydrate-containing compounds play a crucial role in disrupting cell-to-cell and cell-to-matrix interactions and are widely recognized as a key contributor to various diabetic complications. In periodontal tissues, AGEs accumulate at significantly higher levels in diabetic patients compared to non-diabetic individuals.[25] They primarily target collagen, increasing cross-linking and resulting in the formation of rigid, structurally stable collagen macromolecules. Due to their resistance to enzymatic breakdown and normal tissue turnover, these molecules gradually build up, contributing to impaired tissue function and delayed healing.

AGE-collagen levels have been well correlated with the duration of diabetes, diabetic complications, and glycemic control. Moreover, better glycemic control has been associated with a decrease in AGE-collagen formation. AGE-modified bone collagen can influence cellular activity, structural integrity, and overall function, ultimately affecting bone metabolism. Changes in glycation levels within bone collagen appear to disrupt bone turnover, leading to reduced bone formation when AGE accumulation is elevated.[25] This impact has been linked to impaired osteoblastic differentiation and alterations in extracellular matrix production.
Advanced Glycation End Products (AGEs) activate a specific receptor known as the "Receptor for AGEs" (RAGE), which is present on the surface of smooth muscle cells, endothelial cells, neurons, monocytes, and macrophages.[26] This receptor is also expressed in the periodontium, with research showing a 50% increase in RAGE mRNA levels in the gingival tissues of type 2 diabetic patients compared to non-diabetic individuals.

Hyperglycemia leads to heightened RAGE expression and increased AGE-RAGE interactions within the endothelium, which accelerates vascular permeability and promotes thrombus formation. In monocytes, AGE-RAGE interaction induces oxidative stress and activates the transcription factor nuclear factor-kappa B (NF-kB). This activation alters monocyte and macrophage behaviour[27], driving the overproduction of pro-inflammatory cytokines such as IL-16 and TNF-α. The excessive release of these cytokines plays a crucial role in sustaining chronic inflammation, contributing to the development of atheromatous plaques in larger blood vessels.

Elevated oxidative stress has also been observed in the gingival tissues of diabetic patients, correlating with increased accumulation of AGEs. The interaction between AGEs and their receptor, RAGE, within periodontal tissues is believed to contribute to the significantly higher levels of IL-1, TNF-α, and prostaglandin E2 (PGE2) [28] found in the gingival crevicular fluid of diabetic individuals compared to their non-diabetic counterparts.

Additionally, diabetes disrupts the normal balance of collagen turnover. Newly synthesized collagen undergoes rapid degradation due to the increased activity of matrix metalloproteinases (MMPs), while AGE-modified, highly cross-linked collagen macromolecules accumulate in the tissue[29]. This imbalance in collagen metabolism may impair the wound-healing response, making the periodontium more susceptible to damage from chronic microbial insults.

To sum up, the effects of diabetes mellitus on periodontal disease include: -

- Strong association b/w poorly controlled DM & periodontitis. (Nascimento GG, 2018)[30]
- Enlarged gingiva, sessile/pedunculated gingival polyp, abscess formations, periodontitis & loosened teeth. (Pandit et al., 2023)
- Impaired defense mechanisms and heightened vulnerability to infections contribute to the progression of destructive periodontal disease. (Suzanne E. Geerlings, 1999)[31]
- Loe (1993) identified periodontitis as the sixth complication associated with diabetes.[32]

Impact of Diabetes on Periodontal Therapy Outcomes
In well-controlled diabetic patients, the clinical and microbiological response to scaling and root planing (SRP) is comparable to that of non-diabetic individuals, showing notable reductions in probing pocket depth (PPD), clinical attachment loss (CAL), and inflammation. However, in individuals with poorly controlled diabetes, persistent hyperglycemia negatively impacts periodontal therapy outcomes[33] by impairing immune function, slowing collagen turnover, and promoting the accumulation of advanced glycation end products (AGEs). These changes lead to delayed healing, increased inflammatory responses, and a compromised ability to repair periodontal tissues. While some improvement may be observed after SRP, poor glycemic control often results in a rapid recurrence of deep pockets, greater periodontal destruction, and a heightened risk of disease progression. Moreover, the altered oral microbiome in diabetic patients fosters a more pathogenic bacterial environment, further aggravating periodontal breakdown. [34] Successful long-term outcomes in periodontal therapy for diabetic individuals require strict glycemic control, regular periodontal maintenance, and a tailored treatment approach to prevent disease recurrence and complications.

Effect of Periodontitis on Diabetes Mellitus:
As we discussed the consequences of diabetes on periodontium, evidence also shows the possible mechanisms of periodontitis affecting the course of diabetes.

Saengtipbovorn et al. (2014) explored the effects of a comprehensive lifestyle modification and dental care program on elderly patients with Diabetes mellitus (type 2)[35].

The research involved a semi-experimental design with 66 participants in each group receiving either comprehensive intervention or routine care. The intervention included lifestyle and oral health education, individual counseling[35], motivational interviewing, self-regulation guides, and personalized oral hygiene instruction.

After three months, the intervention group showed significant improvements in glycemic control, evidenced by lower HbA1c and fasting plasma glucose levels, as well as enhanced periodontal health, including decreases in plaque accumulation[35], gingival inflammation, pocket depth, clinical attachment loss, and bleeding upon probing.

The findings underscore the impact of comprehensive lifestyle and oral health care in managing diabetes and periodontal health in elderly patients.

Several animal studies have strengthened the association between periodontitis and diabetes mellitus and confirmed that periodontal infection with periodontal pathogens triggers the development of insulin resistance. Periodontitis also aggravates the failure of pancreatic beta-cells in diabetic mice[36]. Many human studies have also proved periodontitis is a risk for diabetes, but the exact mechanism is still unknown.

Multiple clinical studies have investigated the effects of periodontal treatment on enhancing glycemic control in individuals with diabetes.

Research indicates that periodontitis can worsen glycemic control in patients who have diabetes. The chronic inflammation and bacterial infection associated with periodontitis can trigger a systemic inflammatory response[37], leading to elevated levels of inflammatory signaling proteins, such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6).

These cytokines can interfere with insulin signaling pathways, thereby increasing insulin resistance. As a result, maintaining blood sugar levels becomes more challenging for diabetic patients, exacerbating their condition. Apart from periodontal diseases, there is also an increase in circulating TNF-alpha levels in diabetes, including its release from adipose tissues and the stimulation of monocyte-macrophage cell lineage by age.[38]

Furthermore, systemic inflammation triggered by periodontitis can contribute to insulin resistance in non-diabetic individuals, potentially raising their likelihood of acquiring type 2 diabetes. This highlights the crucial role of maintaining periodontal health in both diabetes prevention and overall disease management.

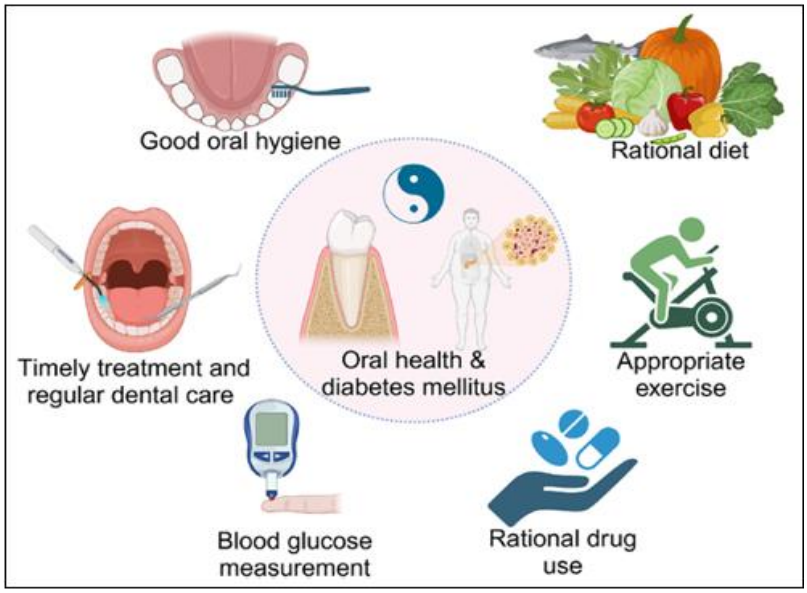

Figure 4: Integrated approach for management of oral health and diabetes mellitus through oral hygiene, dietary control, glycemic monitoring, exercise, drug compliance, and regular dental care.

2. Conclusion

In conclusion, evidence suggests that excessive sugar consumption is pro-inflammatory, disrupts microbial balance, and exhibits addictive properties. These factors promote overconsumption, contributing to systemic risk factors for periodontal inflammation. Periodontal disease progression can also alter the pathophysiology of Diabetes Mellitus. Implementing lifestyle modifications through dietary and nutritional interventions—specifically limiting sugar and ultra-processed food consumption- appears beneficial for periodontal health and warrants further investigation. Public health efforts should focus on educating people about the harmful impacts of consuming too much sugar and encouraging healthier eating habits to enhance overall well-being.

References

[1] Gonzalez JT. Are all sugars equal? Role of the food source in physiological responses to sugars with an

emphasis on fruit and fruit juice. Europe J of Nutri 2024; 63:1435-1451.
[2] Harvard Health Publishing. The Bitter Truth About Added Sugar. 2023. Last assessed on 25/03/2025.
[3] Spencer, Herb. SUGAR: an Essay on THE IMPACT OF SUGAR ON SOCIETY. 2021. Last assessed on 25/03/2025.
[4] American Heart Association. Why sugar matters and how to cut back if you overeat it 2023. Last assessed on 25/03/2025.
[5] Shanmugasundaram S, Karmakar S. Excess dietary sugar and its impact on periodontal inflammation: a narrative review. BDJ Open. 2024:10:78.
[6] World Health Organization. Nutrition in the South-East Asia Region. Geneva: World Health Organization; 2022. Last assessed on 25/03/2025.
[7] Nakrani MN, Wineland RH, Anjum F. Physiology, Glucose Metabolism. 2023. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025.
[8] Rippe JM, Angelopoulos TJ. Relationship between Added sugars Consumption and Chronic Disease Risk Factors: Current Understanding. Nutrients. 2016; 8:697.
[9] Cappelli, D.P., Mobley, C.C. Association between Sugar Intake, Oral Health, and the Impact on Overall Health: Raising Public Awareness. *Curr Oral Health Rep 2017*; **4:176**–183.
[10] Ozougwu JC, Obimba KC, Belonwu CD, Unakalamba CB. Pathophysiology of diabetes mellitus. J Physiol Pathophysiol. 2013; 4:46-57.
[11] Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, Stein C, Basit A, Chan JCN, Mbanya JC, Pavkov ME, Ramachandaran A, Wild SH, James S, Herman WH, Zhang P, Bommer C, Kuo S, Boyko EJ, Magliano DJ. IDF Diabetes Atlas: Global, regional, and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Pract. 2022; 183:109119.
[12] Martha E. Nunn. Understanding the etiologic of Periodontitis: An overview of Periodontal risk Factors. J Periodontol 2000,32, 2003, 11-23.
[13] Cullinan, M., Ford, P., & Seymour, G. Periodontal disease and systemic health: Current status. *Australian Dental Journal*, *54*, S62-S69.
[14] Păunică I, Giurgiu M, Dumitriu AS, Păunică S, Pantea Stoian AM, Martu MA, Serafinceanu C. The Bidirectional Relationship between Periodontal Disease and Diabetes Mellitus-A Review. Diagnostics (Basel). 2023 11; 13:681.
[15] mirrah IN, Lokanathan Y, Zulkiflee I, Wee MFMR, Motta A, Fauzi MB. A Comprehensive Review on Collagen Type I Development of Biomaterials for Tissue Engineering: From Biosynthesis to Bioscaffold. Biomedicines. 2022 ;16; 10:9:2307.
[16] Huang J, Xiao Y, Xu A, Zhou Z. Neutrophils in type 1 diabetes. J Diabetes Investig. 2016; 7:652-63.
[17] Bassani B, Cucchiara M, Butera A, Kayali O, Chiesa A, Palano MT, Olmeo F, Gallazzi M, Dellavia CPB, Mortara L, Parisi L, Bruno A. Neutrophils' Contribution to Periodontitis and Periodontitis-Associated Cardiovascular Diseases. Int J Mol Sci. 2023;19; 24:15370.
[18] Jain A, Chawla M, Kumar A, Chawla R, Grover V, Ghosh S, Pandit N, Chawla P. Management of periodontal disease in patients with diabetes- good clinical practice guidelines: A joint statement by Indian Society of Periodontology and Research Society for the Study of Diabetes in India. J Indian Soc Periodontol. 2020; 24:498-524.
[19] Ryan T. Demmer, Birte Holtfreter, Moïse Desvarieux, David R. Jacobs, Wolfgang Kerner, Matthias Nauck, Henry Völzke, Thomas Kocher; The Influence of Type 1 and Type 2 Diabetes on Periodontal Disease Progression: Prospective results from the Study of Health in Pomerania (SHIP). *Diabetes Care* 2012; 35: 2036–2042.
[20] Paunica I, Giurgiu M, Dumitriu AS, Păunică S, Pantea Stoian AM, Martu MA, Serafinceanu C. The Bidirectional Relationship between Periodontal Disease and Diabetes Mellitus Review. Diagnostics (Basel). 2023;11; 13:681.
[21] Graves DT, Ding Z, Yang Y. The impact of diabetes on periodontal diseases. Periodontol 2000. 2020; 82:214-224.
[22] Malech HL, Deleo FR, Quinn MT. The role of neutrophils in the immune system: an overview. Methods Mol Biol. 2014; 1124:3-10.
[23] Jiao H, Xiao E, Graves DT. Diabetes and Its Effect on Bone and Fracture Healing. Curr Osteoporos Rep. 2015; 13:327-35.
[24] Campos C. Chronic hyperglycemia and glucose toxicity: pathology and clinical sequelae. Postgrad Med. 2012; 124:90-7.
[25] Singh VP, Bali A, Singh N, Jaggi AS. Advanced glycation end products and diabetic complications. Korean J Physiol Pharmacol. 2014; 18:1-14.
[26] Yue Q, Song Y, Liu Z, Zhang L, Yang L, Li J. Receptor for Advanced Glycation End Products (RAGE): A Pivotal Hub in Immune Diseases. Molecules. 2022;2; 27:4922.
[27] González P, Lozano P, Ros G, Solano F. Hyperglycemia and Oxidative Stress: An Integral, Updated and Critical Overview of Their Metabolic Interconnections. Int J Mol Sci. 2023;27; 24:9352.
[28] Shang J, Liu H, Zheng Y, Zhang Z. Role of oxidative stress in the relationship between periodontitis and systemic diseases. Front Physiol. 2023; 14:1210449.
[29] Bondarenko, Larysa. (2019). Diabetes and Collagen: Interrelations. Avicenna Journal of Medical Biochemistry. 7. 64-71.
[30] Nascimento GG, Leite FRM, Vestergaard P, Scheutz F, López R. Does diabetes increase the risk of periodontitis? A systematic review and meta-regression analysis of longitudinal prospective studies. Acta Diabetol. 2018;55(7):653-667.
[31] Könönen E, Gursoy M, Gursoy UK. Periodontitis: a multifaceted disease of tooth-supporting tissues. J Clin Med. 2019;8(8):1135.
[32] Löe H. Periodontal disease: the sixth complication of diabetes mellitus. Diabetes Care. 1993;16(1):329-334.
[33] Yahaya JJ, Doya IF, Morgan ED, Ngaiza AI, Bintabara D. Poor glycemic control and associated factors among patients with type 2 diabetes mellitus: a cross-sectional study. Sci Rep. 2023;14; 13:9673.
[34] Teeuw WJ, Gerdes VE, Loos BG. Effect of periodontal treatment on glycemic control of diabetic patients: a

systematic review and meta-analysis. Diabetes Care. 2010; 33: 421-7.

[35] Saengtipbovorn, S., & Taneepanichskul, S. (2014). Effectiveness of lifestyle change plus dental care (LCDC) program on improving glycemic and periodontal status in the elderly with type 2 diabetes. *BMC Oral Health, 14*, 72.

[36] Liu Y and Zhang Q. Periodontitis aggravated pancreatic beta-cell dysfunction in diabetic mice through interleukin-12 regulation on Klotho. J Diabetes Investing 2016; 7:303-11.

[37] Sanghani NB, Parchwani DN, Palandurkar KM, Shah AM, Dhanani JV. Impact of lifestyle modification on glycemic control in patients with type 2 diabetes mellitus. Indian J Endocrinol Metab. 2013; 17:1030-9.

[38] Al-Mansoori L, Al-Jaber H, Prince MS, Elrayess MA. Role of Inflammatory Cytokines, Growth Factors and Adipokines in Adipogenesis and Insulin Resistance. Inflammation. 2022; 45:31-44.