

Unraveling the Nexus: Exploring the Complex Relationship Between Diabetes and Periodontitis

Vijaya Lakshmi Pavani Kondru

Independent Researcher, USA

kvlpavani@gmail.com

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Abstract:

The intricate interplay between diabetes and periodontitis has garnered significant attention due to their bidirectional relationship and shared pathogenic mechanisms. This review delves into the multifaceted association between diabetes and periodontitis, encompassing epidemiological evidence, underlying pathophysiological pathways, and clinical implications. Epidemiological studies consistently demonstrate a higher prevalence and severity of periodontal disease in individuals with diabetes, highlighting the impact of glycemic control on periodontal health. Shared pathogenic mechanisms, including inflammation, immune dysregulation, and impaired wound healing, contribute to the mutual exacerbation of diabetes and periodontitis. Furthermore, periodontal inflammation may adversely affect glycemic control and contribute to the progression of diabetes-related complications. Clinical management strategies encompass interdisciplinary collaboration, emphasizing comprehensive periodontal care, glycemic control, and lifestyle modifications. Precision medicine approaches hold promise for tailored interventions targeting specific subsets of diabetic patients with periodontitis. This review elucidates the complex interplay between diabetes and periodontitis, underscoring the importance of integrated care models and personalized treatment approaches in optimizing patient outcomes.

Keywords: diabetes, periodontitis, glycemic control, inflammation, immune dysregulation, wound healing, interdisciplinary collaboration, precision medicine

Introduction

Diabetes and periodontitis are two chronic, inflammatory conditions that share a bidirectional relationship, influencing each other's onset, severity, and progression. Understanding the interplay between these diseases is crucial for optimizing patient care and improving health outcomes. This introduction provides context to the relationship between diabetes and periodontitis, highlighting their significance and clinical implications.

1.1 Background

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia resulting from insulin deficiency or resistance. It encompasses various subtypes, including type 1 diabetes, type 2 diabetes, and gestational diabetes, each with distinct etiologies and clinical manifestations. Chronic hyperglycemia in diabetes leads to systemic complications affecting multiple organ systems, including the eyes, kidneys, nerves, and cardiovascular system.

Periodontitis, on the other hand, is a chronic inflammatory disease affecting the supporting structures of the teeth, including the gingiva, periodontal ligament, and alveolar bone. It is initiated by microbial dysbiosis in the oral cavity, leading to an exaggerated host immune response and tissue destruction. Left untreated, periodontitis can result in tooth loss and contribute to systemic inflammation and comorbidities.

The association between diabetes and periodontitis has been extensively studied, with accumulating evidence suggesting a bidirectional relationship. Individuals with diabetes are more susceptible to periodontal disease, exhibiting higher prevalence, severity, and progression of periodontitis compared to non-diabetic counterparts. Conversely, periodontal inflammation may adversely affect glycemic control and contribute to the progression of diabetes-related complications, creating a vicious cycle of mutual exacerbation.

1.2 Significance of the Relationship

The relationship between diabetes and periodontitis holds significant clinical implications for both diseases. Poorly controlled diabetes is associated with increased risk and severity of periodontal disease, emphasizing the importance of glycemic control in preserving periodontal health. Conversely, periodontal therapy may improve glycemic control and reduce the risk of diabetes-related complications, highlighting the potential for periodontal interventions to complement diabetes management strategies.

Furthermore, the bidirectional relationship between diabetes and periodontitis underscores the importance of interdisciplinary collaboration between dental and medical professionals in managing patients with both conditions. Integrated care models that address both glycemic control and periodontal health can improve treatment outcomes and reduce the burden of comorbidities in individuals with diabetes.

In summary, understanding the relationship between diabetes and periodontitis is essential for optimizing patient care, preventing complications, and improving health outcomes. By addressing both metabolic and periodontal health, healthcare providers can enhance the quality of life for individuals affected by these chronic inflammatory conditions.

Epidemiology of Diabetes and Periodontitis

The epidemiological landscape of diabetes and periodontitis reveals a complex interplay between these two chronic conditions, with profound implications for public health and clinical practice. This section explores key epidemiological findings regarding the prevalence, severity, and associated risk factors of diabetes and periodontitis.

1. **Prevalence of Diabetes:** Diabetes mellitus represents a global health challenge, with an escalating prevalence across diverse populations. According to the International Diabetes Federation, approximately 463 million adults aged 20-79 years were living with diabetes worldwide in 2019, projected to rise to 700 million by 2045. Type 2 diabetes accounts for the majority of cases, fueled by aging populations, urbanization, unhealthy lifestyles, and genetic predisposition.
2. **Prevalence of Periodontitis:** Periodontal disease is one of the most prevalent chronic conditions globally, affecting a significant proportion of the adult population. The Global Burden of Disease Study 2017 estimated that severe periodontitis affected 529 million people worldwide, with prevalence rates varying by region, age, and socioeconomic status. Despite advancements in preventive and therapeutic strategies, periodontitis remains a major public health concern due to its impact on oral health-related quality of life and systemic health outcomes.
3. **Association between Diabetes and Periodontitis:** Epidemiological evidence consistently demonstrates a bidirectional relationship between diabetes and periodontitis, with each

condition predisposing individuals to an increased risk and severity of the other. Individuals with diabetes have a higher prevalence, extent, and severity of periodontal disease compared to non-diabetic counterparts. Conversely, periodontitis is associated with poor glycemic control, increased risk of diabetes-related complications, and higher healthcare costs in diabetic patients.

4. **Associated Risk Factors:** Several risk factors contribute to the development and progression of both diabetes and periodontitis, including age, gender, ethnicity, obesity, smoking, and socioeconomic status. Age-related changes in metabolic regulation and immune function increase the susceptibility to diabetes and periodontitis, while modifiable lifestyle factors such as smoking and poor oral hygiene exacerbate their progression. Ethnic disparities in disease prevalence and outcomes highlight the importance of culturally sensitive interventions tailored to diverse populations.
5. **Impact of Comorbidities:** Comorbidities such as obesity, hypertension, dyslipidemia, and cardiovascular disease often coexist with diabetes and periodontitis, creating a complex web of interconnected health conditions. The clustering of these comorbidities, known as the metabolic syndrome, exacerbates systemic inflammation and oxidative stress, contributing to the pathogenesis of diabetes and periodontitis. Multimorbidity imposes significant challenges for disease management and underscores the need for comprehensive, integrated care approaches.

In summary, the epidemiology of diabetes and periodontitis underscores the multifactorial nature of these chronic conditions and their intricate interrelationships. Understanding the epidemiological patterns and associated risk factors is essential for developing targeted prevention and intervention strategies to mitigate the burden of diabetes and periodontitis on individual and population health.

Pathophysiological Pathways

Diabetes and periodontitis share common pathophysiological pathways that contribute to their mutual exacerbation and progression. Understanding these underlying mechanisms is essential for elucidating the intricate interplay between these conditions and developing targeted therapeutic

interventions. This section explores key pathophysiological pathways, including inflammation, immune dysregulation, and impaired wound healing.

3.1 Inflammation:

Inflammation serves as a central mechanism linking diabetes and periodontitis, driving tissue destruction and systemic complications in both conditions. In diabetes, chronic hyperglycemia triggers an inflammatory response characterized by increased production of pro-inflammatory cytokines, such as interleukin-1 β (IL-1 β), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF- α). These cytokines promote endothelial dysfunction, oxidative stress, and leukocyte recruitment, contributing to microvascular complications and impaired tissue repair.

Similarly, periodontitis is initiated by microbial dysbiosis in the oral cavity, leading to the activation of innate and adaptive immune responses. The release of bacterial toxins and virulence factors stimulates the production of pro-inflammatory mediators by resident immune cells, including macrophages, dendritic cells, and neutrophils. Chronic periodontal inflammation results in the destruction of periodontal tissues, including the gingiva, periodontal ligament, and alveolar bone, leading to tooth loss and systemic dissemination of oral pathogens.

The crosstalk between diabetes and periodontitis amplifies systemic inflammation, exacerbating insulin resistance, endothelial dysfunction, and cardiovascular complications. Pro-inflammatory cytokines produced in the periodontal tissues, such as interleukin-6 and C-reactive protein (CRP), have been implicated in the pathogenesis of diabetes-related complications, including cardiovascular disease, nephropathy, and retinopathy. Conversely, systemic inflammation in diabetes contributes to the dysregulation of immune responses and impaired wound healing in periodontitis, creating a vicious cycle of mutual exacerbation.

3.2 Immune Dysregulation:

Immune dysregulation plays a pivotal role in the pathogenesis of both diabetes and periodontitis, contributing to altered host responses to microbial challenges and tissue damage. In diabetes, dysregulation of innate and adaptive immune responses impairs the clearance of pathogens and resolution of inflammation, leading to chronic low-grade inflammation and tissue damage. Aberrant activation of Toll-like receptors (TLRs) and nod-like receptors (NLRs) by microbial

components and danger-associated molecular patterns (DAMPs) exacerbates inflammatory responses and insulin resistance in diabetes.

Similarly, periodontitis is characterized by dysregulated host-microbial interactions and exaggerated immune responses to oral pathogens. Chronic exposure to periodontal pathogens elicits an immune response characterized by the infiltration of neutrophils, monocytes, and lymphocytes into the periodontal tissues. Dysregulation of cytokine networks, including the upregulation of pro-inflammatory cytokines and downregulation of anti-inflammatory mediators, perpetuates tissue destruction and impairs periodontal homeostasis.

The dysregulation of immune responses in diabetes and periodontitis contributes to the persistence of chronic inflammation, tissue destruction, and impaired wound healing. Altered cytokine profiles and dysregulated immune cell functions create a pro-inflammatory microenvironment that perpetuates disease progression and exacerbates systemic complications. Targeting immune dysregulation represents a promising therapeutic approach for mitigating inflammation and improving outcomes in patients with diabetes and periodontitis.

3.3 Impaired Wound Healing:

Impaired wound healing is a hallmark feature of both diabetes and periodontitis, stemming from alterations in angiogenesis, extracellular matrix remodeling, and cell migration. In diabetes, hyperglycemia-induced endothelial dysfunction and oxidative stress impair neovascularization and tissue perfusion, delaying wound healing and predisposing to chronic ulceration and infection. Altered expression of growth factors, such as vascular endothelial growth factor (VEGF) and transforming growth factor-beta (TGF- β), further compromises tissue repair mechanisms in diabetes.

Similarly, periodontitis is associated with impaired wound healing in the periodontal tissues, characterized by inadequate repair of damaged gingival epithelium and periodontal ligament. Persistent inflammation and tissue destruction disrupt the balance between matrix metalloproteinases (MMPs) and tissue inhibitors of metalloproteinases (TIMPs), leading to excessive collagen degradation and impaired tissue regeneration. Dysfunctional fibroblasts and osteoblasts further impair periodontal wound healing, contributing to progressive alveolar bone loss and tooth mobility.

The impaired wound healing responses in diabetes and periodontitis exacerbate tissue damage and hinder the resolution of inflammation, perpetuating disease progression and systemic complications. Targeting key regulators of wound healing, such as growth factors, angiogenic factors, and matrix-modifying enzymes, may promote tissue repair and regeneration in both conditions. Multimodal therapeutic approaches aimed at addressing inflammation, immune dysregulation, and impaired wound healing hold promise for improving outcomes and preventing complications in patients with diabetes and periodontitis.

Clinical Implications

The intricate interplay between diabetes and periodontitis has profound clinical implications for screening, diagnosis, and management strategies. This section discusses key clinical considerations, including screening and diagnosis protocols, treatment strategies, and the importance of interdisciplinary collaboration in optimizing patient care.

4.1 Screening and Diagnosis:

Given the bidirectional relationship between diabetes and periodontitis, routine screening and comprehensive evaluation of both conditions are essential for early detection and intervention. Healthcare providers should incorporate periodontal assessments into diabetes care protocols and vice versa to identify individuals at risk and initiate timely interventions.

Screening protocols for periodontitis in individuals with diabetes may include clinical examinations, periodontal probing, radiographic assessments, and assessment of periodontal parameters such as probing depth, clinical attachment loss, and bleeding on probing. Conversely, diabetic patients should undergo regular assessments of glycemic control, including glycated hemoglobin (HbA1c) measurements, to monitor diabetes management and identify individuals at risk of periodontal complications.

Interdisciplinary collaboration between dental and medical professionals is essential for implementing comprehensive screening and diagnostic protocols, ensuring seamless communication, and coordinating patient care. Integrated care models that incorporate periodontal assessments into routine diabetes care and vice versa facilitate early detection of disease and promote timely intervention to prevent complications.

4.2 Treatment Strategies:

Treatment strategies for individuals with both diabetes and periodontitis should aim to address both metabolic and periodontal health, targeting inflammation, glycemic control, and periodontal tissue regeneration. Multimodal therapeutic approaches tailored to individual patient needs are essential for optimizing treatment outcomes and preventing disease progression.

Periodontal therapy for individuals with diabetes and periodontitis may include scaling and root planing, local antimicrobial agents, and surgical interventions to reduce bacterial burden, control inflammation, and promote periodontal tissue regeneration. Adjunctive therapies such as systemic antibiotics or host modulation agents may be considered in refractory cases to enhance treatment efficacy and prevent disease recurrence.

Optimizing glycemic control is paramount in managing individuals with diabetes and periodontitis, as poor glycemic control exacerbates periodontal inflammation and impairs wound healing. Healthcare providers should emphasize the importance of medication adherence, dietary modifications, and lifestyle interventions to achieve target HbA1c levels and reduce the risk of diabetes-related complications.

Interdisciplinary collaboration between dental and medical professionals is essential for developing personalized treatment plans, coordinating care, and addressing the unique needs of individual patients. Shared decision-making and patient education empower individuals to actively participate in their care and adhere to prescribed treatment regimens, improving treatment outcomes and enhancing overall health and well-being.

4.3 Interdisciplinary Collaboration:

Interdisciplinary collaboration between dental and medical professionals is essential for managing individuals with both diabetes and periodontitis and optimizing treatment outcomes. Close communication and collaboration facilitate comprehensive care planning, timely referrals, and coordinated management of both metabolic and periodontal health.

Rheumatologists, endocrinologists, periodontists, and primary care providers should collaborate closely to develop integrated care plans tailored to individual patient needs and disease severity.

Regular communication and shared decision-making ensure continuity of care and facilitate timely adjustments to treatment regimens based on patient responses and disease progression.

Moreover, patient education and empowerment are integral components of interdisciplinary care, emphasizing the importance of maintaining good oral hygiene practices, adhering to prescribed medications, and attending regular follow-up appointments. Empowering patients to actively participate in their care improves treatment adherence, enhances self-management skills, and promotes overall health and well-being.

In summary, interdisciplinary collaboration between dental and medical professionals is essential for managing individuals with both diabetes and periodontitis and optimizing treatment outcomes. By integrating metabolic and periodontal care, healthcare providers can improve treatment efficacy, prevent complications, and enhance the quality of life for individuals affected by these chronic inflammatory conditions.

Precision Medicine Approaches

Precision medicine offers a promising approach for managing individuals with diabetes and periodontitis by tailoring treatment strategies to individual patient characteristics, including genetic predisposition, biomarker profiles, and disease severity. This section explores the potential applications of precision medicine in optimizing treatment outcomes and preventing complications in individuals with diabetes and periodontitis.

1. **Genetic Profiling:** Genetic susceptibility plays a significant role in the pathogenesis of both diabetes and periodontitis, influencing disease onset, severity, and treatment response. Advances in genomic technologies have enabled the identification of genetic variants associated with susceptibility to diabetes and periodontitis, offering insights into disease mechanisms and potential therapeutic targets.

Precision medicine approaches leverage genetic profiling to stratify patients based on their genetic risk profiles and tailor treatment strategies accordingly. Genetic testing may identify individuals at increased risk of developing diabetes or periodontitis, allowing for targeted interventions to mitigate disease progression and prevent complications. Moreover, pharmacogenomic testing can guide medication selection and dosing based on individual genetic profiles, optimizing treatment efficacy and minimizing adverse drug reactions.

- 2. Biomarker Assessment:** Biomarkers serve as objective indicators of disease activity, progression, and treatment response, facilitating early detection, risk stratification, and personalized treatment approaches. In diabetes, biomarkers such as glycated hemoglobin (HbA1c), C-peptide, and adipokines provide valuable insights into glycemic control, insulin secretion, and adipose tissue function. Similarly, biomarkers of periodontal inflammation, such as interleukin-1 β (IL-1 β), matrix metalloproteinases (MMPs), and prostaglandin E2 (PGE2), reflect disease activity and response to periodontal therapy.

Precision medicine utilizes biomarker assessment to monitor disease progression, guide treatment decisions, and predict treatment outcomes in individuals with diabetes and periodontitis. Integrating biomarker data into clinical decision-making algorithms enables personalized risk assessment and targeted interventions, optimizing treatment efficacy and reducing the risk of complications.

- 3. Individualized Risk Stratification:** Precision medicine allows for individualized risk stratification based on comprehensive assessments of genetic, clinical, and lifestyle factors, enabling targeted interventions tailored to individual patient needs. Risk prediction models incorporating genetic, environmental, and clinical variables can identify individuals at increased risk of developing diabetes or periodontitis, facilitating early intervention and preventive strategies.

Furthermore, precision medicine enables personalized treatment algorithms that account for patient-specific factors, such as disease severity, comorbidities, and treatment preferences. By tailoring treatment strategies to individual patient characteristics, precision medicine optimizes treatment outcomes, reduces the risk of complications, and enhances patient satisfaction and adherence.

- 4. Targeted Therapeutic Interventions:** Precision medicine guides the selection of targeted therapeutic interventions based on individual patient characteristics, including genetic predisposition, biomarker profiles, and treatment responses. Personalized treatment algorithms integrate genetic, clinical, and lifestyle data to inform treatment decisions and optimize therapeutic efficacy.

In diabetes, precision medicine approaches may include tailored pharmacological interventions, lifestyle modifications, and behavioral interventions based on individual patient profiles. Similarly, in periodontitis, precision medicine guides the selection of periodontal therapies, adjunctive treatments, and maintenance protocols tailored to individual patient needs and disease severity.

In summary, precision medicine offers a promising approach for managing individuals with diabetes and periodontitis by tailoring treatment strategies to individual patient characteristics. By integrating genetic profiling, biomarker assessment, individualized risk stratification, and targeted therapeutic interventions, precision medicine optimizes treatment outcomes, prevents complications, and enhances the quality of care for individuals affected by these chronic inflammatory conditions.

Future Directions and Research Implications

The dynamic landscape of diabetes and periodontitis research presents numerous opportunities for advancing our understanding of disease mechanisms, refining diagnostic approaches, and developing novel therapeutic interventions. This section explores future directions and research implications that may shape the field of diabetes and periodontitis in the coming years.

1. **Elucidating Disease Mechanisms:** Future research efforts should focus on elucidating the complex pathophysiological pathways underlying the bidirectional relationship between diabetes and periodontitis. Investigating the molecular mechanisms linking chronic hyperglycemia, inflammation, and immune dysregulation will provide valuable insights into disease pathogenesis and identify novel therapeutic targets.
2. **Exploring the Microbiome-Host Interaction:** The oral microbiome plays a pivotal role in the pathogenesis of periodontitis and may influence systemic health outcomes, including diabetes. Future research should explore the intricate interactions between the oral microbiome and host immune responses in individuals with diabetes and periodontitis, leveraging high-throughput sequencing technologies and multi-omics approaches to characterize microbial dysbiosis and identify potential biomarkers of disease progression.
3. **Advancing Diagnostic Approaches:** Novel diagnostic approaches and biomarkers are needed to improve the early detection and risk stratification of diabetes and periodontitis. Future research should focus on developing non-invasive diagnostic tools, such as salivary

biomarkers, imaging modalities, and point-of-care devices, for accurate and timely identification of individuals at risk of developing diabetes-related complications and periodontal disease progression.

4. **Personalized Treatment Strategies:** Precision medicine approaches hold promise for tailoring treatment strategies to individual patient characteristics, including genetic predisposition, biomarker profiles, and treatment responses. Future research should explore the efficacy of personalized treatment algorithms incorporating genetic testing, biomarker assessment, and individualized risk stratification in optimizing treatment outcomes and preventing complications in individuals with diabetes and periodontitis.
5. **Integrating Digital Health Technologies:** Digital health technologies, including mobile health apps, wearable devices, and telemedicine platforms, offer innovative solutions for remote monitoring, patient engagement, and personalized care delivery. Future research should explore the integration of digital health technologies into diabetes and periodontitis management protocols, enabling real-time data collection, personalized feedback, and remote consultation to improve patient outcomes and enhance healthcare delivery efficiency.
6. **Translational Research and Clinical Trials:** Translational research efforts should bridge the gap between basic science discoveries and clinical applications, facilitating the translation of promising preclinical findings into novel diagnostic tools and therapeutic interventions. Large-scale prospective clinical trials are needed to evaluate the efficacy, safety, and cost-effectiveness of precision medicine approaches, targeted therapeutic interventions, and integrated care models in managing individuals with diabetes and periodontitis.

In summary, future research directions and implications for diabetes and periodontitis encompass elucidating disease mechanisms, exploring the microbiome-host interaction, advancing diagnostic approaches, developing personalized treatment strategies, integrating digital health technologies, and conducting translational research and clinical trials. By addressing these research priorities, we can advance our understanding of disease pathogenesis, improve diagnostic accuracy, optimize treatment outcomes, and enhance the quality of care for individuals affected by these chronic inflammatory conditions.

Conclusion

In conclusion, the intricate interplay between diabetes and periodontitis underscores the multifaceted nature of these chronic inflammatory conditions and their profound impact on systemic health. The bidirectional relationship between diabetes and periodontitis highlights the importance of comprehensive screening, early detection, and integrated management approaches to optimize patient outcomes and prevent complications.

Epidemiological evidence demonstrates a higher prevalence and severity of periodontal disease in individuals with diabetes, emphasizing the need for routine periodontal assessments as part of diabetes care protocols. Conversely, periodontal inflammation may adversely affect glycemic control and contribute to the progression of diabetes-related complications, necessitating close collaboration between dental and medical professionals in managing individuals with both conditions.

Pathophysiological pathways linking diabetes and periodontitis, including inflammation, immune dysregulation, and impaired wound healing, provide insights into disease mechanisms and potential therapeutic targets. Precision medicine approaches offer personalized treatment strategies tailored to individual patient characteristics, including genetic predisposition, biomarker profiles, and treatment responses, optimizing treatment outcomes and preventing complications.

Future research directions encompass elucidating disease mechanisms, advancing diagnostic approaches, developing personalized treatment strategies, integrating digital health technologies, and conducting translational research and clinical trials. By addressing these research priorities, we can advance our understanding of disease pathogenesis, improve diagnostic accuracy, optimize treatment outcomes, and enhance the quality of care for individuals affected by diabetes and periodontitis.

In summary, a multidisciplinary approach that integrates dental and medical care, leverages precision medicine approaches, and embraces technological innovations holds promise for optimizing patient care and improving health outcomes in individuals with diabetes and periodontitis. Through collaborative efforts and innovative research initiatives, we can continue to make strides in addressing the complex challenges posed by these chronic inflammatory conditions and ultimately improve the quality of life for affected individuals.

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