

The Impact of Diabetes Mellitus on Apical Periodontitis: Insights from Animal and Human Studies

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Abstract

Objective: This review examines the interrelation between diabetes mellitus (DM) and apical periodontitis (AP), explaining key biological mechanisms and summarizing the main findings from animal and human studies.

Methods and Results: A comprehensive literature search was conducted across PubMed, Scopus, and Web of Science, focusing on peer-reviewed studies published over the last two decades. Several studies have shown that hyperglycemia impairs VEGF-regulated angiogenesis, reduces osteoblast activity, and maintains elevated levels of inflammatory cytokines such as TNF- α and IL-6, thereby increasing periradicular lesion size and delaying tissue healing. Diabetic animal models showed reduced bone density, increased vascular calcification, and accelerated progression from caries to pulp necrosis. Clinically, T2DM (type 2 diabetes mellitus) was associated with higher AP prevalence, greater bacterial endotoxin load, and lower root-canal success rates. These effects were magnified by poor glycemic control.

Conclusion: Diabetes mellitus exacerbates AP through impaired angiogenesis, dysregulated immune response, and impaired bone metabolism. To reduce these risks, strategies such as strict blood glucose control, enhanced antimicrobial disinfection, minimally invasive interventions, and the use of bioactive materials are recommended. Future research should explore how controlling oral infections impacts systemic metabolic health. Investigating the role of bioactive materials and anti-inflammatory treatments in improving AP outcomes is also essential. (**International Journal of Biomedicine. 2026;16(1):6-13.**)

Keywords: diabetes mellitus • periapical periodontitis • animal experimentation • root canal therapy

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Abbreviations

AP, apical periodontitis; **BMD**, bone mineral density; **BMP-2**, bone morphogenetic protein-2; **CT**, computed tomography; **DM**, diabetes mellitus; **DXA**, dual-energy X-ray absorptiometry; **ET**, endodontically treated; **MTA**, mineral trioxide aggregate; **T1DM**, type 1 diabetes mellitus; **T2DM**, type 2 diabetes mellitus; **VEGF**, vascular endothelial growth factor; **VEGFA**, vascular endothelial growth factor A; **VEGFR2**, vascular endothelial growth factor receptor 2.

Introduction

Diabetes mellitus (DM) is a long-term metabolic condition characterized by elevated blood glucose levels due to abnormalities in insulin function and/or production.¹ This disease has multiple consequences, including retinopathy, nephropathy, neuropathy, angiopathy, and impaired wound healing.^{2,3} Studies also highlight the association between DM and periodontitis.^{4,5} Among the many oral complications associated with DM, apical periodontitis (AP), an inflammatory disorder

of the periapical tissues typically resulting from untreated dental pulp infections,^{6,7} stands out due to its prevalence and impact on endodontic outcomes.^{8,9} In Europe, AP affects about 61% of the population, with prevalence increasing with age, while endodontic treatment rates are estimated at around 41%.¹⁰

The relationship between DM and AP is of particular concern because of the altered immune responses associated with diabetes, which may exacerbate the severity of AP and complicate its treatment.¹¹ Clinical observations and epidemiological surveys increasingly suggest that patients with

DM experience a higher frequency of AP, larger osteolytic lesions, and slower periapical healing than subjects with normal blood glucose levels.¹² Proposed biological links include dysregulated innate immunity, chronic hyperglycemia, and the accumulation of AGEs (advanced glycation end-products), each of which may disrupt vascular integrity, bone remodeling, and cytokine profiles in periapical tissues.¹²⁻¹⁵

To better understand the biological interplay between DM and AP, researchers have increasingly relied on both animal models and clinical studies. Rodent models, particularly diabetic rats, have proven invaluable due to their anatomical and physiological similarities to human dentition and their controlled experimental conditions.¹⁶ Experimental work by Uysal et al.¹⁷ and Takashima et al.¹⁸ in these models has suggested that hyperglycemia may impair angiogenesis, delay tissue repair, and alter inflammatory signaling in oral tissues. In addition, studies indicate that diabetes may influence mandibular and alveolar bone development, with reduced bone density that could, in turn, affect endodontic treatment outcomes.¹⁹⁻²¹ Some studies also suggest that DM may worsen AP by increasing inflammation around the root tip, enlarging lesion size, and slowing the healing process.²²

Based on the available evidence, this narrative review comprehensively explores the interrelationship between DM and AP, synthesizing key findings from both animal and human studies. Despite growing interest in this field, the underlying mechanisms remain incompletely understood, and published data often vary in methodological quality.¹² This review examines the impact of diabetes on angiogenesis, bone remodeling, inflammatory responses, and endodontic treatment outcomes in the context of apical periodontitis. A better understanding of these relationships is crucial for developing more effective treatment strategies and improving endodontic care for patients with diabetes.

Materials and Methods

A structured narrative literature review was conducted to explore the relationship between DM and AP. The literature search was performed across three major databases: PubMed, Web of Science, and Scopus. A combination of Medical Subject Headings (MeSH) and free-text terms was used to build the search queries. Boolean operators structured the search logic. A representative PubMed query was: (“Diabetes Mellitus” [MeSH Terms]) AND (“Periapical Periodontitis” [MeSH Terms] OR “Apical Periodontitis” [All Fields]) AND (“Root Canal Therapy” [MeSH Terms]) AND (“Animal Experimentation” [MeSH Terms] OR “Humans” [MeSH Terms]) AND (English [Filter]). Additional keywords included “angiogenesis,” “bone remodeling,” “VEGF,” and “pulpal healing,” and filters were applied to prioritize peer-reviewed articles with full-text access.

Studies were included if they were experimental or clinical investigations published in English between 2005 and 2025, assessed the effects of type 1 diabetes mellitus (T1DM) or type 2 diabetes mellitus (T2DM) on pulpal or periapical tissues, evaluated angiogenesis, inflammatory markers, or bone turnover in the context of AP, and employed validated

methodologies such as histological, immunohistochemical, radiographic, or molecular techniques. Both animal and human studies were eligible, provided they included appropriate control groups.

Exclusion criteria comprised studies lacking diabetic comparison groups or clinical diabetic parameters (e.g., HbA1c), research limited to periodontal disease without apical or pulpal analysis, non-mammalian models, and non-original publications such as reviews, abstracts, or editorials. Studies with small sample sizes (fewer than 10 animals or 20 human participants) and studies lacking control groups were also excluded.

The initial search identified 70 records (33 from PubMed, 19 from Web of Science, and 18 from Scopus). After title and abstract screening, 41 full-text articles were assessed. After applying inclusion and exclusion criteria, 23 studies were selected for final synthesis, comprising 11 animal and 12 human studies. Thematic analysis was used to categorize the included studies into three domains: (1) vascular effects focusing on angiogenic markers and microvascular changes; (2) bone remodeling covering osteoblast and osteoclast activity and alveolar bone integrity; and (3) apical periodontitis progression addressing lesion development, inflammatory cytokine profiles, and healing outcomes following endodontic treatment.

Results

Vascular Changes and Angiogenic Dysregulation in Diabetic Dental Pulp

Animal Studies

Multiple studies have investigated how DM affects dental pulp regeneration, focusing on changes in angiogenesis and growth factor expression. In a study using Goto-Kakizaki (GK) rats as a model for T2DM, Martinho et al.²³ observed significantly elevated fasting glycemia and triglyceride levels ($P < 0.001$; $P < 0.05$), along with larger apical periodontitis lesions compared to healthy controls ($P < 0.05$). VEGF levels were also significantly lower in diabetic rats than in Wistar rats ($P < 0.05$), and unlike the control group, the diabetic animals did not exhibit an increase in VEGF expression following the induction of apical periodontitis.

In contrast, Uysal et al.¹⁷ observed elevated VEGF and CD68 expression in the pulp of streptozotocin-induced diabetic rats, alongside dilated blood vessels and increased hemorrhage. Ilić et al.²⁴ demonstrated that direct pulp capping in diabetic rats produced a peak VEGF level of 19.3 ± 0.9 pg/mg on Day 1 ($P < 0.001$), with a delayed increase in BMP-2 by Day 7. Additionally, sustained hyperglycemia in SDT-fatty rats (Spontaneously Diabetic Torii) led to progressive pulpal calcification starting at week 6, as observed by Takashima et al.,¹⁸ with the authors attributing these changes to AGEs and vascular fragility.

Human and In Vitro Evidence

Human histological data mirror findings in animal models. In a comparative human study, VEGF and BMP-2 levels were measured in dental pulp samples from 28 healthy

and 28 T2DM patients using ELISA. Diabetic patients exhibited significantly higher concentrations of both growth factors in intact pulp tissue compared to healthy controls. Following indirect pulp capping, VEGF and BMP-2 levels decreased markedly in both groups. The Kruskal–Wallis test confirmed statistically significant differences in VEGF and BMP-2 levels among the study groups ($P<0.001$).²⁵ Another study found that although VEGFA, a key proangiogenic factor, was actively transcribed and translated under hyperglycemic conditions, its primary receptor, VEGFR2, was absent in all diabetic samples. Additionally, dental pulp cell viability was significantly reduced at high glucose concentrations (25 mM) compared to controls ($P=0.005$).²⁶

In a pilot study comparing clinically normal teeth from T2DM and non-diabetic patients, diabetic pulps showed reduced vascularity, increased calcification, and thickened vessel walls. Immunohistochemical markers of inflammation were significantly elevated in the diabetic group (e.g., CD68, $P<0.001$; IL-6, $P<0.0001$; TNF- α , $P=0.01$), while regulatory FOXP3 expression was significantly lower ($P=0.01$).²⁷

Alveolar Bone Remodeling and Bone Loss

Animal Models

In a study by Yilmaz et al.,¹⁹ streptozotocin-induced diabetic rats exhibited significantly elevated blood glucose levels compared to controls ($P<0.05$). Histological analysis revealed vascular dilation and hemorrhage in the periodontal membrane, along with increased inflammatory cell infiltration. Osteonectin expression was positive in the periodontal ligament but absent in alveolar bone osteocytes. At the same time, osteopontin showed strong positivity in fibroblasts, collagen fibrils of the periodontal membrane, and the alveolar bone matrix.

Abbassy et al.²⁰ reported significantly reduced mineral apposition and bone formation rates in Wistar rats with T1DM. Additionally, micro-CT analysis revealed a significant deterioration in bone quality, characterized by reduced trabecular bone volume and increased trabecular separation in the T1DM group. Statistical analysis showed a significantly higher number of osteoclasts in the control group than in the T1DM group ($P<0.05$).

Hendrijantini et al.²¹ investigated the effects of DM and osteoporosis on mandibular bone remodeling in Wistar rats over a 12-week period. The study included control, diabetic, and osteoporotic groups. Results showed that the diabetic group exhibited the lowest levels of Osterix expression, a key transcription factor in osteoblast differentiation. In addition, both the diabetic and osteoporotic groups demonstrated a significant reduction in the osteoblast/osteoclast ratio compared to controls.

Human Clinical and Radiographic Studies

In a retrospective study of 124 patients, Tabassum et al.²⁸ reported significantly greater mean alveolar bone loss in patients with T2DM than in non-diabetic individuals (3.07 \pm 1.14 mm vs. 2.59 \pm 1.08 mm, $P=0.018$), and a higher prevalence of moderate-to-severe periodontitis in the diabetic group. Exceptionally few

case-control studies have examined the relationship between diabetes mellitus and the severity of mean alveolar bone loss. Kayal et al.²⁹ observed greater alveolar bone loss in diabetic patients (3.59 \pm 1.37 mm) than in controls (2.66 \pm 1.05 mm, $P=0.001$). This pattern was consistent across both genders and age groups. Tooth loss was significantly more prevalent among individuals with diabetes, particularly those aged over 55 or with more than 10 missing teeth.

In contrast, Ay et al.³⁰ found no statistically significant differences in mandibular BMD (bone mineral density) between patients with T2DM and healthy individuals. The study included 19 diabetic participants and 17 control subjects matched by age and sex. Panoramic radiographs calibrated with a DXA phantom were used for quantitative analysis, and BMD measurements were performed using Scion Image software on digitized images. The mean mandibular BMD values in diabetic women and men were 1.53 \pm 0.27 g/cm² and 1.52 \pm 0.29 g/cm², respectively, compared to 1.56 \pm 0.28 g/cm² and 1.46 \pm 0.23 g/cm² in controls.

Development and Severity of Apical Periodontitis

Animal Studies

In streptozotocin-induced diabetic rats, significantly larger periradicular lesions were observed at both 21 and 40 days following pulp exposure ($P<0.05$), accompanied by greater tissue destruction and inflammatory exudate compared to non-diabetic controls.²² Similarly, GK rats with T2DM developed more extensive bone resorption and larger periapical lesions, especially when maintained on a high-sucrose diet.³¹

Prasetyo et al.³² showed that LPS (lipopolysaccharide)-induced AP in diabetic rats led to elevated inflammatory markers. IL-6 expression increased significantly only by Day 42 ($P<0.05$), whereas TNF- α was elevated as early as Day 14 and remained sustained through Day 42. There were significant differences between the control and experimental groups ($P<0.05$).

Another model using WBN/KobSlc diabetic rats showed faster progression of caries to pulp necrosis and periapical inflammation than controls. Lesion severity strongly correlated with caries extent, and the inflammatory process extended into periapical tissues, resulting in pronounced alveolar bone resorption.³³

Human Studies

Clinical research aligns with animal models, showing increased AP prevalence and severity in individuals with diabetes. In a retrospective study, Segura-Egea et al.³⁴ reported that 81.3% of T2DM patients had at least one tooth with AP, compared with 58% in non-diabetic controls ($P=0.040$; OR=3.2). Additionally, 6.9% of all teeth examined in diabetic patients had AP, compared with 4% in controls ($P=0.007$), and the average number of teeth with AP was higher in diabetics (1.5 \pm 1.1) than in controls (0.9 \pm 1.1).

Subsequent cross-sectional studies reinforced this association. One study found that T2DM was significantly associated with AP (OR=2.05; 95% CI: 1.73–2.43), particularly

in patients with poor glycemic control ($HbA1c > 8.0$; $OR = 2.46$). Conversely, metformin and statin therapy were each independently associated with a lower AP prevalence.³⁵

Using cone-beam CT, Barros et al. reported that 64.8% of diabetic participants had periapical index scores ≥ 4 , compared with 17.7% of controls ($P < 0.05$). Diabetic canals had higher bacterial and endotoxin levels, which correlated with larger lesion size ($P < 0.05$).³⁶

Radiographic surveillance in a separate study revealed that AP was significantly more prevalent in T2DM patients (74%) than in non-diabetic controls (42%) ($P = 0.002$), and root-filled teeth were also more common among diabetics (70% vs. 50%, $P = 0.043$). Multivariate logistic regression, adjusted for the number of teeth, confirmed that both periapical status ($P = 0.0071$) and the number of root-filled teeth ($P = 0.0035$) were significantly associated with diabetic status. Additionally, persistent AP in root-filled teeth was observed more frequently in diabetic patients (46%) than in controls (24%), although this difference was not statistically significant ($P > 0.05$).³⁷ In addition to prevalence data, outcome-based studies further support this association. Martinho et al.²³ reported a significantly lower success rate following root canal treatment in diabetic patients compared to healthy control patients ($P < 0.001$).

The influence of glycemic control on apical periodontitis outcomes was clearly demonstrated in this analysis. Patients with poorly controlled diabetes showed a significantly higher prevalence of AP lesions (18.29%) compared to well-controlled diabetics (9.21%). Diabetic patients had more endodontically treated teeth (ET) than nondiabetic patients, with averages of 4.18% versus 1.82%, respectively. Furthermore, the AP/ET ratio was higher in diabetics (27.7%) than in nondiabetics (19.3%).³⁸

Discussion

Diabetes Mellitus and Pulpal Angiogenesis

Ethical and practical limitations limit the ability to conduct in vivo studies of dental pulp repair processes in humans, necessitating the use of animal models that may not fully mimic human biological responses to diabetes and dental pulp injury. The animal studies consistently demonstrate that DM impairs angiogenic signaling and compromises dental pulp healing. In diabetic rat models, VEGF expression remains suppressed even after AP induction, suggesting a deficient angiogenic response that may contribute to delayed tissue repair.²³ Conversely, other animal studies have reported increased expression of VEGF and CD68 in diabetic pulp tissue, accompanied by dilated blood vessels and hemorrhage, which may reflect dysregulated inflammatory angiogenesis rather than effective neovascularization.¹⁷ Temporal disruptions in key regenerative markers have also been observed. In particular, VEGF levels have been shown to peak prematurely, whereas BMP-2 exhibits a delayed increase following pulp-capping procedures, indicating altered timing and dynamics of repair.²⁴

This experimental evidence finds support in clinical observations. Human studies have revealed that, despite elevated VEGF and BMP-2 levels in intact diabetic pulp tissue,

their reduction following indirect pulp capping may reflect a diminished reparative capacity in hyperglycemic conditions. The consistent pattern of change between the two growth factors across both diabetic and healthy samples suggests that they may act in a coordinated manner during pulp tissue response, regardless of baseline concentration differences.²⁵ The absence of VEGFR2 expression in hyperglycemic conditions, despite VEGFA upregulation, further highlights a disrupted downstream angiogenic response, which could compromise vascular regeneration. This dissociation implies that even when angiogenic mediators are present, the downstream signaling or cellular responsiveness is compromised, likely due to hyperglycemia-induced receptor downregulation.²⁶

Additionally, diabetic pulp tissues consistently exhibit heightened inflammation, vascular calcification, and reduced cellularity, all of which suggest compromised tissue homeostasis and impaired immune regulation. However, the supporting in vitro study included only 20 extracted molars, 10 from well-controlled T2DM patients and 10 from non-diabetics, limiting statistical power and generalizability.²⁷ Supporting these findings, another study reported that DM appears to increase inflammation, degeneration, and mineralization in the pulp tissue while reducing cell proliferation, emphasizing the complex pathological alterations driven by hyperglycemia.³⁹

These cumulative findings underscore the complex interplay among hyperglycemia, vascular dysfunction, and inflammation in undermining pulp vitality and regeneration in individuals with diabetes. Clinically, this disrupted healing response helps explain the increased risk of endodontic failure and slower recovery observed in diabetic patients.

Alveolar Bone Remodeling and Bone Loss in Diabetes Mellitus

The collective evidence indicates that DM disrupts bone remodeling through impaired vascular integrity, altered inflammatory responses, and suppression of osteogenic signaling pathways. Findings suggest that chronic inflammation under hyperglycemic conditions delays osteoblast differentiation and inhibits normal bone formation.¹⁹ A rat model of diabetes showed a marked reduction in the osteoblast-to-osteoclast ratio and the lowest Osterix expression among all experimental groups, indicating impaired osteoblast maturation. Although the study's interpretation is limited by the differing observation periods between the diabetes and osteoporosis models, the findings still reinforce the notion that diabetes compromises mandibular bone remodeling by downregulating osteogenic signaling pathways.²¹

Another study similarly reported that DM significantly impairs mandibular bone formation and alters bone microarchitecture, as evidenced by decreased mineral apposition and bone formation rates in diabetic rats compared to the control group. Additionally, the findings indicated fewer osteoclasts in the diabetic group, suggesting diminished bone resorption activity. This imbalance between bone formation and resorption may contribute to a state of osteopenia in the diabetic rats, highlighting the adverse effects of diabetes on craniofacial bone health.²⁰ The research focused on a specific age range of rats (3 to 8 weeks old) to observe dynamic changes

in bone formation, which may limit the generalizability of the findings to other age groups or species, as bone formation and turnover rates can vary significantly with age and developmental stage.

Clinical evidence suggests that T2DM is associated with more severe alveolar bone loss and a higher risk of periodontitis progression.⁴⁰ Studies reinforce that diabetic individuals are more susceptible to periodontal destruction and tooth loss, likely due to chronic inflammatory and metabolic disturbances.^{28,29} Diabetes has an essential effect on enhancing osteoclastogenesis and on increasing osteoblast apoptosis. Interestingly, the impact of diabetes on bone loss and coupled bone formation is likely to involve its effects on both innate and adaptive immune responses.^{41,42}

In contrast, Ay et al.³⁰ found no statistically significant difference in BMD between diabetic and non-diabetic subjects. However, this finding may reflect the limited sensitivity of panoramic radiographs to detect early diabetes-induced changes, rather than a genuine absence of bone alterations. The small sample size and lack of microstructural analysis further limit the generalizability of these results. Advanced imaging, such as CBCT or DXA, may better capture early diabetic bone alterations.

These vascular and bone-related alterations driven by chronic hyperglycemia likely contribute to the progression of periodontal disease and compromise the regenerative capacity of alveolar bone in individuals with diabetes.

Experimental and Clinical Evidence Linking Diabetes Mellitus to Apical Periodontitis

Animal studies provide compelling evidence that DM exacerbates both the development and severity of AP through multiple pathological mechanisms. Investigations using streptozotocin-induced diabetic rats demonstrated significantly larger periradicular lesions and a reduced defensive capacity against microbial pathogens.²² In Goto-Kakizaki rats, systemic hyperglycemia combined with a high-sucrose diet further amplified bone resorption and lesion size, indicating a synergistic effect between metabolic imbalance and dietary factors.³¹ LPS-induced models show a delayed yet sustained rise in TNF- α and IL-6 under diabetic conditions, reflecting a defective inflammatory resolution.³² Experimental DM also accelerates progression from caries to pulp necrosis and AP, with lesion severity closely paralleling caries extent.³³

Clinical studies support these experimental findings. A retrospective cohort study reported AP in 81.3% of individuals with T2DM, compared with 58% of normoglycemic controls, establishing DM as an epidemiological risk factor. The study's exclusion of patients with seven or fewer remaining teeth aimed to reduce confounding by periodontal disease, but it may limit generalizability to the broader diabetic population.³⁴

A large cross-sectional analysis showed that T2DM is independently associated with increased AP prevalence. Notably, poor glycemic control, as reflected by elevated HbA1c levels, was associated with an even greater risk, suggesting that metabolic instability exacerbates periapical disease. In contrast, the use of metformin and statins appeared to have a protective effect: both treatments were associated with a lower

prevalence of AP, possibly due to their anti-inflammatory or glycemic-modulating effects. Because the study was cross-sectional, it cannot establish a causal relationship between T2DM and AP and may be influenced by unspecified factors such as diet or genetics. Additionally, reliance on medical records and a single hospital network limits data accuracy and generalizability.³⁵

Cone-beam CT and microbiological assessments have linked T2DM to higher bacterial and endotoxin loads, contributing to more severe periapical bone destruction and potentially affecting endodontic treatment outcomes.³⁶ Long-term radiographic surveillance has demonstrated that diabetic patients harbor more root-filled teeth and experience a greater likelihood of persistent periapical inflammation.³⁷

The role of glycemic regulation was further underscored by evidence that poorly controlled diabetics show a higher prevalence of AP and a higher AP/ET ratio compared to well-controlled patients, highlighting the negative impact of uncontrolled diabetes on dental health. However, the cross-sectional design, small sample size, and reliance on radiographic diagnosis limit the ability to draw causal inferences and generalisability.³⁸ Finally, outcome-based research has demonstrated significantly lower root canal success rates in diabetic patients compared to normoglycemic individuals, reinforcing diabetes as a negative prognostic factor.²³

Additionally, a cross-sectional study analyzing full-mouth radiographs from a Brazilian population found that AP was significantly more prevalent in untreated teeth of T2DM patients (10%) than in those of nondiabetics (7%), supporting the hypothesis that diabetes may act as a disease modifier in the development of primary endodontic disease. However, no significant difference in AP prevalence was found between the two groups in root canal-treated teeth, suggesting that diabetes may not adversely affect post-treatment healing. These findings align with previous clinical research showing increased AP prevalence in diabetics but mixed evidence regarding endodontic treatment outcomes.⁴³

Taken together, evidence from both experimental and clinical studies indicates that DM increases the prevalence, severity, and progression of AP. Prolonged inflammation (e.g., sustained TNF- α and IL-6), greater microbial burden, impaired immune responses, and reduced post-treatment healing capacity all contribute to this elevated risk. These findings underscore the need for strict glycemic control and individualized treatment planning in the endodontic management of diabetic patients.

Management Strategies for Diabetic Patients Undergoing Endodontic Therapy

Endodontic management in diabetic patients requires a comprehensive approach that addresses both systemic and local factors. Given their heightened risk of delayed healing and infection, maintaining optimal glycemic control is essential to improve treatment outcomes.⁴⁴ Research has shown that patients with well-controlled DM exhibit better healing responses and lower complication rates than those with poor control.⁴⁵ Therefore, close collaboration with the

patient's primary care physician or endocrinologist to stabilize glycemic status before and after endodontic treatment is critical.

Another key management strategy involves enhanced antimicrobial protocols to mitigate the increased risk of infection in diabetic patients. Because of their compromised immune response, higher concentrations of sodium hypochlorite and adjunctive agents such as chlorhexidine or calcium hydroxide may be recommended to improve canal disinfection.⁴⁶ Additionally, due to the delayed healing observed in diabetic tissues, minimally invasive approaches such as smaller access cavities and conservative root canal instrumentation can help preserve tooth structure and reduce post-operative complications.⁴⁴

To improve endodontic outcomes in diabetic patients, adjunctive use of NSAIDs (nonsteroidal anti-inflammatory drugs) can help manage post-operative inflammation. Ibuprofen 600 mg, alone or combined with acetaminophen 1000 mg, is effective for short-term pain relief, though optimal dosing strategies for prolonged pain control remain unclear.⁴⁷ Given the impaired healing dynamics in diabetes, using biomaterials with proven bioactivity and immunotolerance, such as MTA (mineral trioxide aggregate), may help mitigate the risks of delayed tissue repair and chronic inflammation. Thus, the selection of bioactive materials should be considered a key component of endodontic management in this patient population. MTA is suitable for diabetic patients, as preclinical studies show that it maintains biocompatibility and promotes mineralization regardless of diabetic status. In rats, Angelus MTA® induced similar mineralized tissue formation and mild inflammation in both diabetic and non-diabetic groups, supporting its use in regenerative endodontic procedures.⁴⁸

Patient education is also essential. Informing diabetic patients about the importance of blood glucose control, adherence to medications, and compliance with post-treatment care can significantly enhance treatment outcomes.⁴⁹

Limitations

While this review offers a comprehensive synthesis of current evidence, certain limitations should be acknowledged. First, as a narrative review, it does not follow the rigorous methodology of a systematic review or meta-analysis, which may introduce some selection bias despite predefined inclusion and exclusion criteria. Second, the body of evidence is highly heterogeneous: studies vary in animal models, diabetic subtypes, diagnostic protocols, and outcome measures, making direct comparisons difficult and weakening the generalizability of overarching conclusions. Translational challenges further complicate interpretation. Most animal studies employ streptozotocin-induced or genetic models (e.g., GK, SDT rats) that mimic T1DM or exaggerated metabolic states, whereas most clinical cases involve T2DM with variable glycemic control, obesity, and systemic inflammation. Additionally, key clinical variables, such as medication regimens and diabetes duration, are seldom reported or controlled in human studies, limiting causal inference. Finally, many animal and in-vitro investigations rely on small sample sizes, which reduces

statistical power and makes it harder to apply the findings to human clinical scenarios.

Conclusion

This review highlights the complex interplay between diabetes mellitus and apical periodontitis, demonstrating that hyperglycemia impairs angiogenesis, suppresses bone remodeling, elevates pro-inflammatory cytokines, and delays periapical healing. Both animal and human studies confirm that diabetic patients are more prone to larger lesions, poorer healing outcomes, and lower root canal treatment success rates.

To reduce these risks, endodontic care for diabetic patients should prioritize strict glycemic control, enhanced antimicrobial disinfection, minimally invasive techniques, and the use of bioactive materials such as MTA. Adjunctive anti-inflammatory therapies (e.g., NSAIDs) may help reduce post-operative complications, especially in patients with pre-existing inflammation. Diabetic individuals should be treated as a high-risk group, with individualized protocols and close coordination between dental and medical providers.

Future research should explore how controlling oral infections impacts systemic metabolic health. Research into the role of bioactive materials and anti-inflammatory drugs in improving treatment outcomes for apical periodontitis is also essential. Strengthening our understanding of this oral-systemic connection will help optimize care for individuals with diabetes.

Conflicts of Interest

The authors declare that they have no competing interests.

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