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Periapical healing outcome following non-surgical endodontic intervention among diabetic patients: A systematic review conducted according to PRISMA guidelines and the Cochrane handbook for systematic reviews of interventions

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ABSTRACT

Background: Periapical diseases are common dental conditions that require non-surgical endodontic intervention (NEI) for successful treatment. However, the impact of diabetes mellitus (DM) on the periapical healing (PH) outcome in diabetic patients remains somewhat unclear. This review aimed to evaluate the PH outcome following endodontic intervention among DM-afflicted individuals.

Methods: A comprehensive search was conducted across multiple electronic databases to identify relevant studies. Specifically, a set of selection criteria was applied to select studies that assessed PH outcomes in individuals with DM who underwent different treatment protocols. Data extraction and quality assessment were performed following predetermined protocols. The risk of bias (RoB) 2 assessment tool evaluated the quality of the included studies.

Results: A total of 11 studies met the inclusion criteria and were included in the investigation. Four studies showed a higher incidence of apical periodontitis in diabetic individuals compared to controls, and five studies reported reduced healing and success rates in this group. Overall, nine studies have shown that DM has a negative impact on periapical outcomes. This suggests that DM is an important factor in the prognosis of endodontic intervention. The assessment tools used were PAI, PR, SC, and FD analysis. RoB-2 assessed the included studies as having a moderate RoB.

Conclusion: This review provides compelling evidence that DM patients experienced a noticeable negative impact on PH outcomes compared to the control population. These findings highlight the importance of considering the diabetic status of patients when assessing the prognosis of periapical diseases and planning interventions for NEI. Further research is needed to validate these results and explore potential mechanisms underlying the observed associations.

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1. Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by impaired insulin function or insulin resistance, resulting in high glucose (HG) levels (Palumbo et al., 2018). It is a significant global health concern, affecting millions of individuals worldwide (Cho et al., 2018). DM has been associated with various complications, including those affecting oral health (Grisi et al., 2022). Symptoms of DM develop gradually, and some individuals may not experience noticeable symptoms for years. These symptoms include fatigue and weakness, recurrent infections, tingling or numbness, and frequent infections. Periapical diseases (PDs) are common dental conditions characterized by inflammation and infection in the tissues surrounding the root apex (Couto et al., 2021). These conditions can lead to significant pain, swelling, and even tooth loss if left untreated (Jiang and Liang, 2022)Inchingolo et al., 2011.Table 1.

Periapical healing (PH) refers to the biological process through which the periapical tissues surrounding the root apex of a tooth undergo repair and restoration after receiving endodontic treatment (Khandelwal et al., 2022). It is a crucial outcome measure in assessing the success of root canal therapy, as it indicates the resolution of inflammation, elimination of microbial infection, and regeneration of the periapical tissues (Holland et al., 2017).

The healing of periapical tissues involves a complex interplay of various biological events, including immune response, tissue repair, and remodeling processes (Alghamdi et al., 2020). After the elimination of bacteria and infected tissues through root canal treatment, the periapical region initiates a series of healing responses (Kumar et al., 2021). Initially, an acute inflammatory reaction occurs, characterized by the influx of immune cells, such as neutrophils and macrophages, to the site of infection (Kumar et al., 2021). These cells play a pivotal role in phagocytizing bacteria and removing necrotic debris. As the acute inflammation subsides, the healing process transitions to a reparative phase. Fibroblasts and undifferentiated mesenchymal cells migrate to the periapical region and begin synthesizing extracellular matrix components, including collagen fibers and proteoglycans (Glera-Swarez et al., 2022). This extracellular matrix provides structural support and serves as a scaffold for subsequent tissue regeneration. Angiogenesis, which refers to the formation of new blood vessels, is another crucial aspect of PH (Joshi et al., 2020). The restoration of an adequate blood supply is essential for delivering oxygen, nutrients, and immune cells to the healing site. Endothelial cells proliferate and form new capillaries, facilitating the recruitment of fibroblasts and enhancing the regenerative potential of the periapical tissues (Ferrandez et al., 2021; Minervini et al., 2023c). Over time, the reparative phase progresses into the remodeling phase, characterized by the maturation and organization of the newly formed tissue (Ferrnadez et al., 2021). The collagen fibers become more organized, and the architecture of the periapical region begins to resemble that of healthy periapical tissues. This remodeling process continues gradually, leading to the restoration of normal periapical anatomy (Chung et al., 2019).

Understanding the impact of DM on PH outcomes following a single-sitting, non-surgical endodontic intervention (NEI) is of utmost importance in dental practice. While several studies have investigated this relationship (Balsera et al., 2019; Segura-Egea et al., 2015, 2016), there is still a need to synthesize the existing evidence and provide a clearer understanding of the association between DM and PH outcomes. Hence, this review was undertaken to answer the research question: "What is the periapical outcome in diabetic individuals undergoing single-sitting, non-surgical endodontic treatment?"

Table 1
Abbreviations used in this review.

Term	Abbreviation used
Non-surgical endodontic intervention	NEI
Periodontal disease	PD
Periapical healing	PH
Periapical radiograph	PR
Control group	CG
Diabetes mellitus	DM
Periapical index	PAI
Apical periodontitis	AP
Strindberg's criteria	SC
Periapical lesions	PL
Type 2 diabetes mellitus	T2DM
Root canal	RC
Hyperglycemia	HG
Fractal Dimension	FD

2. Materials and methods

2.1. Eligibility criteria

A specific PICO strategy was utilized to formulate a focused research question and guide the review process.

Population (P) – Patients diagnosed with DM.

Intervention (I) – The intervention was endodontic treatment, specifically for those who required non-surgical intervention.

Comparison (C) – The comparison group included non-diabetic controls.

Outcome (O) – The primary outcome of interest was the rate of pH and success of endodontic treatment.

The study adopted the following inclusion and exclusion criteria. These criteria were carefully designed to ensure the selection of relevant studies while excluding those that did not meet the specified criteria.

Inclusion Criteria: (1) Original research studies, including randomized controlled trials (RCTs), prospective or retrospective cohort studies, and case-control studies; (2) Patients with DM who have PD or are undergoing RC therapy; (3) Studies using clinical and radiographic evaluations; and (4) Studies published in English (to ensure accurate interpretation and synthesis of the findings).

Exclusion Criteria: (1) Irrelevant Studies: Studies that did not address the specific research question or failed to meet the inclusion criteria; (2) Studies conducted on animal models or *in vitro* experiments; (3) Case reports, reviews, and conference abstracts; and (4) Studies published in languages other than English.

2.2. Search strategy

This review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) strategy (Arya et al., 2021). The review is being submitted for PROSPERO registration. A comprehensive database search strategy was employed across various databases, as presented in Table 2. The search strategy utilized MeSH keywords and Boolean operators to ensure a systematic and thorough retrieval of relevant studies. The search strategy utilized a combination of MeSH terms and keywords related to diabetes, endodontic treatment, and PH. The keywords included variations of terms such as "diabetes," "endodontics," "periapical healing," "single-visit" and their respective synonyms. Boolean operators, such as "AND" and "OR," are used to combine search terms and refine search results.

2.3. Data extraction

The data extraction protocol for this investigation was developed to systematically collect relevant information from the selected studies. Table 3 shows the data on study characteristics, including author ID, publication year, study design, and geographic location of the study. The technical information of the included studies is presented in Table 4. Three reviewers collected the data separately, and a fourth reviewer was consulted in case of any discrepancies.

Table 2
Search strategy implementation across different databases.

Database	Search Terms	Boolean Operators
PubMed	("Diabetes Mellitus" OR "Diabetes Mellitus, Type 2″ OR "Diabetes Mellitus, Type 1″) AND ("Endodontics" OR "Root canal Therapy") AND ("Periapical Healing" OR "Periapical Diseases") AND ("Single-Visit" OR "One-Visit" OR "One-Appointment")	AND
Embase	('diabetes mellitus'/exp OR 'diabetes mellitus type 2'/exp OR 'diabetes mellitus type 1'/exp) AND ('endodontics'/exp OR 'Root canal therapy'/exp) AND ('periapical healing'/exp OR 'periapical diseases'/exp) AND ('single-visit' OR 'one-visit' OR 'one-appointment')	AND
Scopus	(INDEXTERMS('diabetes mellitus') OR INDEXTERMS('diabetes mellitus type 2') OR INDEXTERMS('diabetes mellitus type 1')) AND (INDEXTERMS('endodontics') OR INDEXTERMS('Root canal therapy')) AND (INDEXTERMS('periapical healing') OR INDEXTERMS('periapical diseases')) AND (INDEXTERMS('single-visit') OR 'one-visit' OR 'one-appointment')	AND
Web of Science	TS=("diabetes mellitus" OR "diabetes mellitus type 2″ OR "diabetes mellitus type 1″) AND TS=("endodontics" OR "Root canal therapy") AND TS=("periapical healing" OR "periapical diseases") AND TS=("single-visit" OR "one-visit" OR "one-appointment")	AND
Cochrane Library	(("diabetes mellitus": MeSH) OR ("diabetes mellitus, type 2″: MeSH) OR ("diabetes mellitus, type 1″: MeSH)) AND (("endodontics": MeSH) OR ("Root canal therapy": MeSH)) AND (("periapical healing": MeSH) OR ("periapical diseases": MeSH)) AND (("single-visit" OR "one-visit" OR "one-appointment"))	AND
CINAHL	(MH "Diabetes Mellitus" OR MH "Diabetes Mellitus, Type 2″ OR MH "Diabetes Mellitus, Type 1″) AND (MH "Endodontics" OR MH "Root canal Therapy") AND (MH "Periapical Healing" OR MH "Periapical Diseases") AND (MH "Single-Visit" OR "One-Visit" OR "One-Appointment")	AND
ProQuest	(diabetes mellitus OR diabetes mellitus type 2 OR diabetes mellitus type 1) AND (endodontics OR Root canal therapy) AND (periapical healing OR periapical diseases) AND (single-visit OR one-visit OR one-appointment)	AND

2.4. Quality assessment

The bias assessment for the studies selected in this review was conducted using the risk of bias (RoB) 2.0 tool (McGuiness et al., 2021; Sterne et al., 2019) to evaluate the strength of the evidence and the reliability of the findings reported in the systematic review. Each domain was evaluated based on specific signaling questions and the corresponding response options, which enabled an assessment of the RoB for each study. Two reviewers independently assessed the bias. Any discrepancies or disagreements were resolved through discussion and consensus.

Table 3
Assessment of demographic variables selected for the review.

Study ID	Year	Region	Sample size (n)	Age range (in years)	Gender ratio
Arya et al [20]	2017	India	21	30–65	12 males
Britto et al [21]	2003	USA	30	39–84	14 males
Ferreira et al [22]	2014	Portugal	23	Unspecified	10 males
Fouad et al [23]	2003	USA	129	Unspecified	Unspecified
Lopez et al [24]	2011	Spain	50	36–83	20 males
Marotta et al [25]	2012	Brazil	30	40–69	12 males
Rudranaik et al [26]	2016	India	40	39 (mean)	28 males
Segura et al [27]	2005	Spain	70	61.0 ± 8.4 (mean)	29 males
Smadi et al [28]	2017	Jordan	145	50.3 ± 8.91 (mean)	Not specified
Ugur Aydin et al [29]	2019	Turkey	37 patients; 46 M	38 + 6.5 (diabetics)	Not specified
Laukkanen et al [30]	2019	Helsinki	41	51.5 + 15.0	51% males

3. Results

3.1. Study characteristics

The search yielded 738 articles. A total of 11 studies were included in the final analysis (Alsomadi, 2017; Arya et al., 2017; Britto et al., 2003; Ferreira et al., 2014; Fouad and Burleson, 2003; Laukkenen et al., 2019; López-López et al., 2011; Marotta et al., 2012; Rudranaik et al., 2016; Segura-Egea et al., 2005; Uğur Aydın et al., 2021) that investigated the impact of DM on periapical health following NEI across different regions. The overall findings revealed that the studies encompassed a diverse range of sample sizes and age groups, with some studies specifying the gender ratio. The gender distribution varied across the studies, with a majority of female participants being diabetic. The included studies were reported from different regions, such as India, the United States, Portugal, Spain, Brazil, Jordan, China, Turkey, and Helsinki. Table 3 displays a comprehensive overview of the studies projecting sample sizes, age ranges, and gender ratios across different regions.

3.2. Main findings

Table 4 presents an overview of multiple studies investigating the impact of DM on periapical outcomes following endodontic intervention. Of the 11 studies, nine of them exhibited a significant relationship between diabetic patients and periapical outcomes. The success rate and healing rate in diabetics were lower in these studies as compared to their controls. Four studies [24–26, 29] showed greater occurrence of apical periodontitis, and five of them (Alsomadi, 2017; Arya et al., 2017; Laukkenen et al., 2019; Rudranaik et al., 2016; Segura-Egea et al., 2005; Uğur Aydın et al., 2021) showed reduced healing and success rates as compared to controls. The synthesized results suggest that the success of NEI is compromised in patients with DM. Different diagnostic assessment tools were used: PAI, PR, SC, and FD.

Arya et al. (2017) conducted a prospective study comparing DM patients (n = 21) to a control group (CG) (n = 25). PAI was used as a diagnostic assessment tool, and a 12-month follow-up period was implemented. The study found that DM had a detrimental effect on the success of NEI. Britto et al. (2003) conducted a cross-sectional study comparing DM patients (n = 30) to a CG (n = 23). They used PR as a diagnostic tool, although the follow-up period was unspecified. The study observed a higher likelihood of PL in men with T2DM who

Table 4
Assessment of PH-related variables selected for the review.

Study ID	Protocol	Groups assessed	Diagnostic assessment tool	Follow-up period (in months)	Inference observed
Arya et al [20]	Prospective	DM (n = 21) and CG (n = 25)	PAI	12	In terms of PH, DM had a deleterious effect on the success of NEI. Biomarkers in T2DM patients were not improved by nonsurgical treatments. 43% of diabetic samples healed as compared to 80 % in the control section.
Britto et al [21]	Retrospective	DM (n = 30) and CG (n = 23)	PR and SC	Unspecified	No effect of diabetes on periapical outcome was noticed
Ferreira et al [22]	Retrospective	DM (n = 23) and CG (n = 23)	PAI and PR	Unspecified	No significant difference was noted between the groups at 0.830.
Fouad et al [23]	Prospective	DM (n = 459) and CG (n = 72)	PR and Orstavile PAI	>24 months	In situations of PL, NEI was less likely to be successful in DM patients due to greater rates of PD in their teeth. DM group reported with 31% and control group with 38% with AP
Lopez et al [24]	Cross-sectional	DM (n = 50) and CG (n = 50)	PAI and PR	Unspecified	AP was noted in 74% of diabetics as compared to 42% of controls (OR −3.9), significant at p = 0.002.
Marotta et al [25]	Cross-sectional	DM (n = 30) and CG (n = 60)	PR and SC	Unspecified	An enhanced prevalence of AP among diabetics (15%) was exhibited, suggesting a strong and statistically significant association with T2D at p = 0.05
Rudranaik et al [26]	Prospective	DM (n = 30) and CG (n = 30)	PR and SC	12	Patients with T2DM exhibited a pronounced presence of chronic and significantly enlarged PL in comparison to the CG group. Notably, individuals with inadequate glycemic control demonstrated a distinct pattern of PL deterioration.
Segura et al [27]	Cross-sectional	DM (n = 38) and CG (n = 32)	PAI and PR	Unspecified	A substantially greater prevalence of AP was strongly linked to T2DM.
Smadi et al [28]	Cross-sectional	DM (n = 145) and CG (n = 146)	PAI and PR	Unspecified	The results elucidated a significantly augmented prevalence of AP in DM sufferers (13.5%) in comparison to the CG (11.9%), accompanied by an escalated incidence of enduring chronic AP.
Ugur Aydin et al [29]	Retrospective	DM (n = 46) and CG (n = 52)	PAI and Fractal dimension (FD) analysis	12	FD analysis showed significantly better healing in controls (0.274 + 0.08) as compared to diabetics (0.180 + 0.114) at p < 0.05
Laukkanen et al [30]	Retrospective	DM (n = 41) and CG (n = 284)	PAI and PR	6 – 71 months	Success rate in diabetics was 73.2% as compared to 85.6% of controls significant at p = 0.043

underwent NEI. Ferreira et al. (2014) conducted a cross-sectional study comparing DM patients (n = 23) to a CG (n = 23). They used PAI and PR as diagnostic tools, but the follow-up period was unspecified. The findings of this investigation were inconclusive regarding the rising prevalence of AP in DM patients. Fouad and Burleson (2003) conducted a retrospective study comparing DM patients (n = 459) to a CG (n = 72). They used PR as a diagnostic tool and had a follow-up period of over 24 months. The study indicated that in cases of PL, NEI was less likely to be successful in DM patients due to higher rates of PD in their teeth. Lopez et al. (2011) conducted a cross-sectional study comparing DM patients (n = 50) to a CG (n = 50). They utilized PAI and PR as diagnostic tools, although the follow-up period was unspecified. The study demonstrated a significantly higher prevalence of AP in patients with T2DM, indicating a strong association between the two. Marotta et al. (2012) conducted a cross-sectional study comparing DM patients (n = 30) to a CG (n = 60). They used PR and clinical examination (SC) as diagnostic tools, but the follow-up period was unspecified. The study revealed an increased prevalence of AP, which exhibited a statistically significant association with T2DM. Rudranaik et al. (2016) conducted a prospective study comparing DM patients (n = 30) to a CG (n = 30). They employed PR and SC as diagnostic tools and had a 12-month follow-up period. The study found that patients with T2DM exhibited a higher prevalence of chronic and significantly enlarged PL compared to the CG. Notably, individuals with inadequate glycemic control demonstrated a distinct pattern of PL deterioration. Segura et al. (2005) conducted a cross-sectional study comparing DM patients (n = 38) to a CG (n = 32). They used PAI and PR as diagnostic tools, but the follow-up period was unspecified. The study revealed a significantly higher prevalence of AP, strongly associated with T2DM. Smadi et al. (2017) conducted a cross-sectional study comparing DM patients (n = 145) to a CG (n = 146). They used PAI and PR as diagnostic tools, although the follow-up period was unspecified. The results indicated a significantly higher prevalence of AP in DM patients compared to CG. This was accompanied by a greater incidence of chronic AP. Uğur Aydın et al. (2021) compared 46 M from diabetic patients with 52 M from the CG. PR and FD assessed the periapical outcome after 12 months. FD analysis showed healing in both groups, but it was more pronounced in the diabetic group. Laukkanen et al. (2019) compared 41 diabetic individuals with 284 control subjects. Diabetes compromised the outcomes of the RCT during the follow-up period.

3.3. Risk of bias assessment

Overall, the quality of the evaluated studies was of moderate risk. None of the studies determined sample size calculations, so the potential for selection bias was unclear. Confounding factors such as the duration of diabetes and the quality of dental fillings were not addressed in any of the studies, which resulted in an unclear risk score for other biases. Laukkanen et al. (2019) was the only study that considered other systemic conditions, but it was performed by dental students. This compromised the quality of the study in terms of the assessed outcomes, as shown in Figs. 1 and 2.

4. Discussion

The study's findings highlight the importance of considering the DM status of patients when planning and performing endodontic interventions. Dental professionals should be aware of the potential challenges associated with PH in DM patients and implement appropriate strategies to optimize treatment outcomes. Future studies should aim to elucidate the underlying mechanisms through which DM affects PH and explore potential interventions to improve healing outcomes in diabetic patients. Additionally, investigating the impact of different levels of diabetic control, duration of diabetes, and the role of specific treatment modalities on PH would provide valuable insights for clinical decision-making(Ali et al., 2023; Lo Giudice and Machado, 2023; Makanjuola and Deb, 2023; Marwan and Todo, 2022; Polychronakis et al., 2023; Romanos et al., 2023; Santos et al., 2023). The findings also call for enhanced interdisciplinary collaboration between dental and medical professionals. Recognizing the systemic implications of DM on

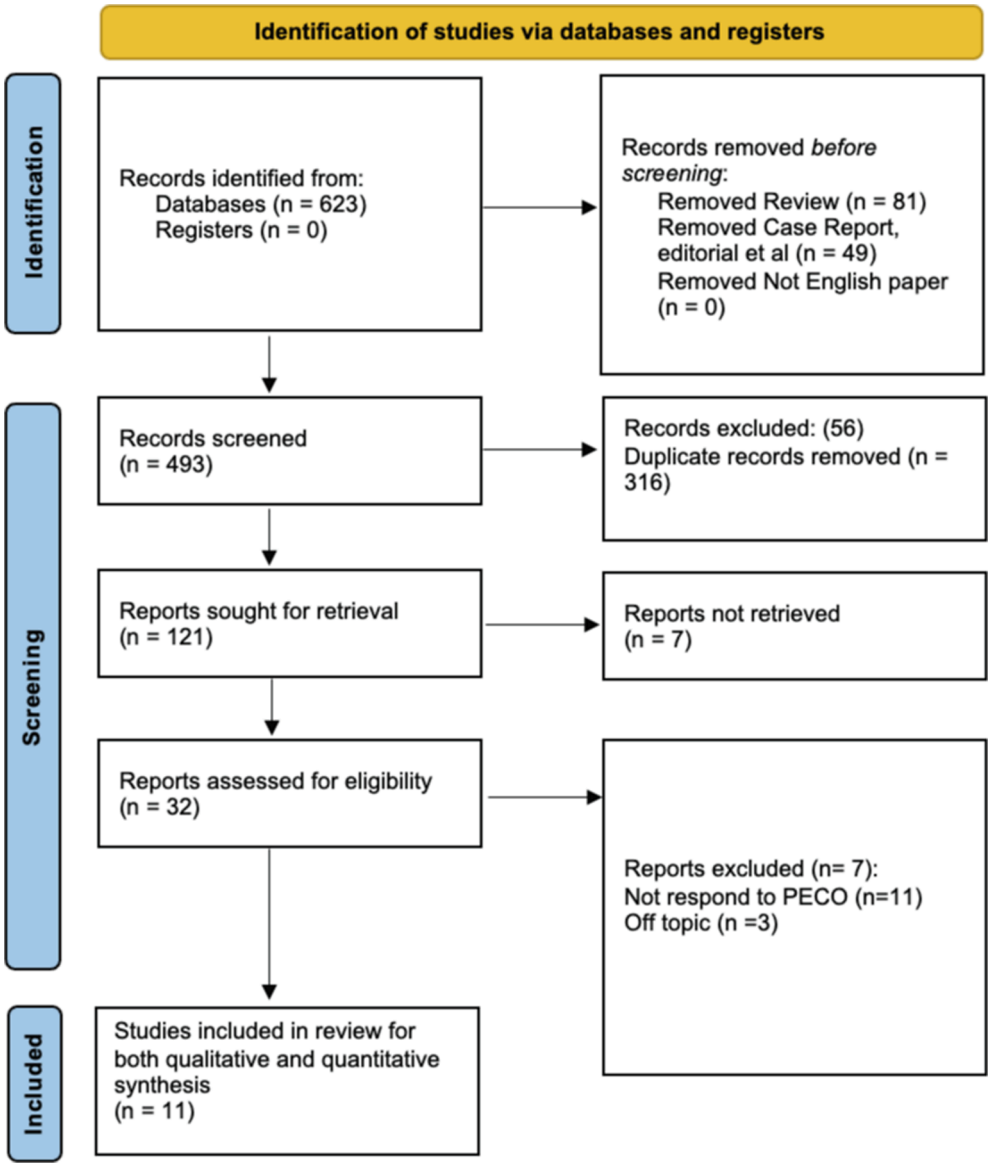

Fig. 1. Graphical representation of the PRISMA guideline utilisation in the review.

oral health and PH underscores the importance of a comprehensive approach to patient care. Collaboration between dental and medical practitioners can facilitate better management of diabetic patients, considering their overall health status and optimizing treatment outcomes. Ultimately, the significance of these findings lies in their potential to improve patient care and enhance treatment outcomes for diabetic individuals who require endodontic interventions. By recognizing the impact of DM on PH, dental professionals can tailor their treatment strategies and provide more targeted care to diabetic patients.

An important observation in the study conducted by Arya et al. (2017) was the increase in HbA1C levels over time in 16 out of 21 diabetic patients. Males in the study by Britto et al. (2003) showed a greater predilection for residual lesions. This was the only study that excluded defective restorations, which could result in coronal leakage. The age group of the experimental group was higher in diabetics, which could be attributed to the fact that the disease tends to occur in later stages of life, as observed in the study conducted by Ferreira et al. (2014). Patients in the study carried out by Fouad and Burleson (2003) were either treated in a single visit or in multiple visits. Endodontists were regularly trained and calibrated. It also reported the positive outcome of endodontic intervention between the pre-operative and post-operative phases. In the study by López-López et al. (2011), diabetic cohorts experienced a significantly higher rate of tooth loss. The mean number of teeth present in diabetics was 21.9 ± 6.4, compared to 24.6 ± 3.8 in controls. The endodontists who assessed the condition in Marotta et al. (2012) were calibrated and showed good agreement, with a kappa value of 0.84. Smadi et al. (2017) showed that poorly controlled DM had a higher prevalence compared to well-controlled DM (18.29 versus 9.21). Fractal dimension analysis was done by Uğur Aydın et al. (2021). The same size and position of the ROI were maintained in pre- and post-treatment radiographs, ensuring standardization. A radiologist, along with two endodontists, assessed the radiographs in the study conducted by Laukkanen et al. (2019).

Dental implants, the temporomandibular joint (TMJ), and PH (associated with endodontic therapy) are all related in the context of oral health and comprehensive dental rehabilitation (Minervini et al., 2023c; Nicholson et al., 2022). According to the findings of another investigation (Khandelwal et al., 2022), the combined odds ratio (OR) suggested a higher prevalence of PL in patients with DM compared to a CG. This finding aligns with the results of multiple studies (Aminoshariae et al., 2017; Khalighinejad et al., 2016; Vlassara, 1997), which cited different cross-sectional studies of varying methodological quality

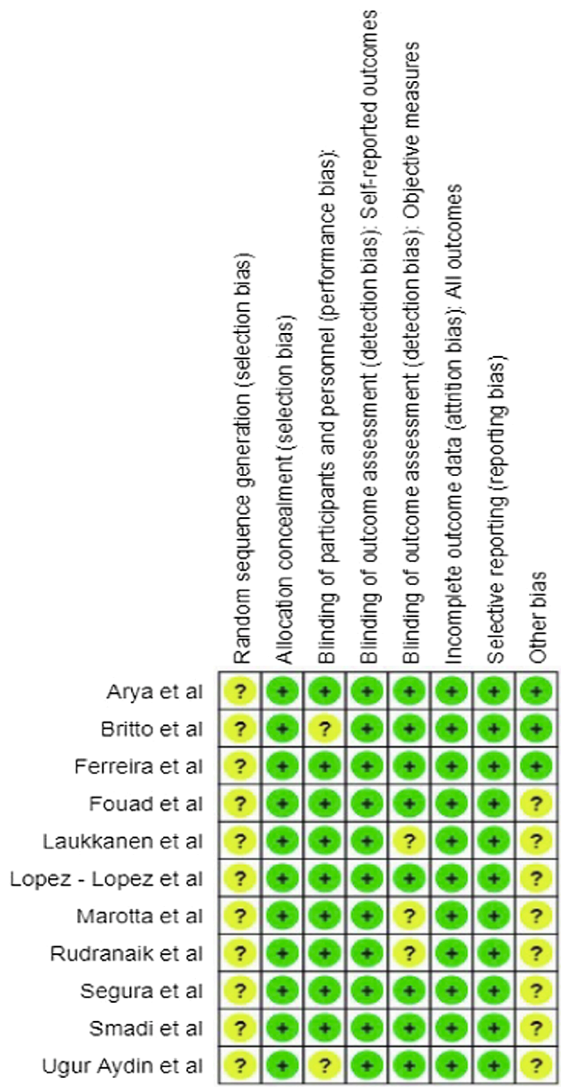

Fig. 2. Risk of bias summary of included studies.

and lacked robust evidence. It has been observed that the reactivation of intercellular pathways can trigger an elevation in pro-inflammatory cytokines, as demonstrated by a couple of studies (Al-Zahrani et al., 2017; Tanaka et al., 2013). Consequently, individuals with DM experience compromised immune responses and reduced tissue repair capacity, particularly in relation to the periapical condition of root-filled teeth. The upregulation of pro-inflammatory chemical mediators contributes to impaired bone turnover rates and delayed wound healing processes. A recent review (Alghamdi et al., 2020) focused on evaluating the effectiveness of secondary root canal treatment in individuals with a specific medical condition. The findings indicated a positive correlation between the presence of DM and an increased incidence of unretrieved root-filled teeth. Different studies (Al-Zahrani et al., 2017; Gilbert et al., 2010; Mindiola et al., 2006; Ng et al., 2011) have provided insights into the association between DM and the likelihood of retaining root-filled teeth. Several other investigations included in this review comprised cohort-based studies, offering a robust foundation for estimating the impact of a specific risk factor on the healing process (Britto et al., 2003; Laukkenen et al., 2019; López-López et al., 2011; Minervini et al., 2023c; Segura-Egea et al., 2005). These studies serve as important initial benchmarks in understanding the relationship between risk factors and healing outcomes.

Another systematic review (Gupta et al., 2020) conducted on similar grounds to ours assessed the association between DM and the extent of PL in root-filled teeth. The pooled ORs for observational studies and clinical studies were 1.42 and 6.36, respectively, indicating a higher prevalence of PL among DM subjects. These findings suggest that DM may have an impact on the healing outcome of RC treatment, increasing the likelihood of PL in DM patientsCantore et al., 2014.

It is essential to compare the results of studies with those of individuals without DM to evaluate the impact of diabetes on PH following single-visit endodontic treatment. This exact methodology was adopted in one of the papers included in this review (Laukkanen et al., 2019), which included both DM and non-DM patients. The study reported comparable success rates between the two groups. This suggests that single-visit endodontic treatment may have similar efficacy in promoting PH in both categories of individuals.

A study by Sisli et al. (2019) investigated the PH outcome in diabetic patients using cone-beam computed tomography (CBCT) imaging. The finding indicates a slightly lower success rate compared to non-DM individuals. The study also highlighted the potential influence of DM-related factors, such as HG levels and microvascular complications, on the healing process. In contrast, another study (Trope et al., 1999) reported positive outcomes in DM patients who underwent single-visit endodontic treatment. The study utilized PR. The researchers emphasized the importance of comprehensive patient management, including glycemic control and adherence to oral hygiene practices, in achieving successful PH outcomes in DM patients. These findings support the notion that diligent management of DM-related factors may enhance the success rate of single-visit endodontic treatment in DM individuals.

It is important to note that the assessment methods employed in these studies contribute to the variations in reported success rates. While PR is commonly used, CBCT imaging provides a more detailed and accurate evaluation of PH. Studies utilizing CBCT imaging allow for a more comprehensive assessment of healing outcomes, including the evaluation of three-dimensional changes in tissues (Mindiola et al., 2006). The use of CBCT imaging may reveal subtle healing changes that could be overlooked in two-dimensional radiographs. Therefore, future studies incorporating advanced imaging techniques could provide valuable insights into the PH outcome in DM patients (Minervini et al., 2023a, 2023b; Sisli, 2019; Di Stasio et al., 2018)Wang et al., 2014.

Moreover, considering the systemic health status and overall well-being of DM patients is crucial in interpreting the results of these studies. DM is a multifactorial disease with varying levels of severity and complications among individuals (Palumbo et al., 2018). Factors such as the duration of diabetes, glycemic control, the presence of comorbidities, and systemic medications may influence the healing capacity and response to endodontic treatment (Cho et al., 2018). Future studies should consider comprehensive patient profiles and subgroup analyses to evaluate the impact of these factors on PH outcomes in this specific type of population (Grisi et al., 2022).

Treatment of periapical lesions in diabetic patients can be challenging due to the complex interplay between diabetes and oral health. Diabetes, particularly uncontrolled diabetes, may compromise the immune system's ability to fight infections. This makes them more susceptible to oral infections. Impaired immune function may also slow down the body's natural ability to resolve the infection, thereby increasing the risk of treatment failure and recurrence. Another important factor to consider is delayed wound healing, which can affect the healing process following endodontic treatment for periapical lesions. The body's ability to repair damaged tissues and resolve the infection may be compromised, potentially leading to prolonged discomfort and a higher risk of complications. Furthermore, poorly managed diabetes increases the risk of complications. In the context of periapical lesions, untreated or poorly managed infections can worsen and become more challenging to control, potentially resulting in cellulitis, abscess formation, or osteomyelitis.

Despite the beneficial information gained from this investigation, there are certain limitations that should be acknowledged. The reliance on published studies introduces the possibility of selection bias. The

studies included in the systematic review may not represent the entire body of literature on the topic. Some relevant studies may have been missed due to the search strategy or exclusion criteria, which could introduce a potential bias in the results. Furthermore, the quality of the studies included is an important consideration. The RoB assessment can be conducted using tools such as RoB 2.0, which can provide insights into the methodological quality of the studies. However, the quality of the available studies varied, and limitations in study design, potential confounders, or inadequate reporting may have an impact on the reliability and validity of the findings. Lastly, the generalizability of the findings may be limited to specific populations or settings. The included studies might have focused on specific patient populations or geographical regions, which may not fully represent the diverse population of diabetic patients. Therefore, caution should be exercised when extrapolating the findings to different populations or clinical contexts.

5. Conclusion

This review provides valuable insights into the impact of DM on PH outcomes following non-surgical endodontic visits. The findings indicate that DM has a noticeable effect on PH, resulting in a decreased likelihood of favorable outcomes compared to non-DM individuals. These findings have important clinical implications, suggesting that diabetic patients may require special considerations and interventions to optimize PH outcomes. However, it is crucial to acknowledge the limitations of this study, including heterogeneity among the included studies, selection bias, and variations in study quality. Despite the fact that glycemic control seems to be a key factor in treatment success, the dearth of high-quality studies in this field emphasizes the need for further research. To enhance the possibility of successful endodontic treatment outcomes in diabetic patients, dental professionals should prioritize comprehensive diabetes management as an essential aspect of patient care. The most effective management of diabetes before and after endodontic procedures depends on close collaboration between dental specialists, endocrinologists, and diabetic care teams. Multidisciplinary collaboration is necessary to provide optimal patient care.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

Al-Zahrani, M.S., Abozor, B.M., Zawawi, K.H., 2017. The relationship between periapical lesions and the serum levels of glycosylated hemoglobin and C-reactive protein in type 2 diabetic patients. Saudi Med. J. 38 (1), 36–40. https://doi.org/10.15537/smj.2017.1.16052.

Alghamdi, F., Alhaddad, A.J., Abuzinadah, S., 2020. Healing of periapical lesions after surgical endodontic retreatment: a systematic review. Cureus. https://doi.org/10.7759/cureus.6916.

Ali, A, Bassir, H, Delgado-Ruiz, R, 2023. Influence of the Printing Orientation on Parallelism, Distance, and Wall Thickness of Adjacent Cylinders of 3D-Printed Surgical Guides. Prosthesis 5 (1), 310–326. https://doi.org/10.3390/prosthesis5010023.

Alsomadi, L., 2017. Apical periodontitis and endodontic treatment in patients with type II diabetes mellitus: comparative cross-sectional survey. J. Contemp. Dental Pract. 18 (5), 358–362. https://doi.org/10.5005/jp-journals-10024-2046.

Aminoshariae, A., Kulild, J.C., Mickel, A., Fouad, A.F., 2017. Association between systemic diseases and endodontic outcome: a systematic review. J. Endod. 43 (4), 514–519. https://doi.org/10.1016/j.joen.2016.11.008.

Arya, S., Duhan, J., Tewari, S., Sangwan, P., Ghalaut, V., Aggarwal, S., 2017. Healing of apical periodontitis after nonsurgical treatment in patients with type 2 diabetes. J. Endod. 43 (10), 1623–1627. https://doi.org/10.1016/j.joen.2017.05.013.

Britto, L.R., Katz, J., Guelmann, M., Heft, M., 2003. Periradicular radiographic assessment in diabetic and control individuals. Oral Surg., Oral Med., Oral Pathol., Oral Radiol., Endodontol. 96 (4), 449–452. https://doi.org/10.1016/S1079-2104(03)00034-9.

Cantore, S., Mirgaldi, R., Ballini, A., Coscia, M.F., Scacco, S., Papa, F., Inchingolo, F., Dipalma, G., De Vito, D., 2014 May 1. Cytokine gene polymorphisms associate with microbiogical agents in periodontal disease: our experience. Int J Med Sci. 11 (7), 674–679. https://doi.org/10.7150/ijms.6962. PMID: 24843315; PMCID: PMC4025165.

Cho, N.H., Shaw, J.E., Karuranga, S., Huang, Y., da Rocha Fernandes, J.D., Ohlrogge, A. W., Malanda, B., 2018. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res. Clin. Pract. 138, 271–281. https://doi.org/10.1016/j.diabres.2018.02.023.

Di Stasio, D., Romano, A., Gentile, C., Maio, C., Lucchese, A., Serpico, R., Paparella, R., Minervini, G., Candotto, V., Laino, L., 2018. Systemic and topical photodynamic therapy (PDT) on oral mucosa lesions: an overview. J Biol Regul Homeost Agents. 32 (2 Suppl. 1), 123–126. PMID: 29460529.

Fouad, A.F., Burleson, J., 2003. The effect of diabetes mellitus on endodontic treatment outcome. J. Am. Dent. Assoc. 134 (1), 43–51. https://doi.org/10.14219/jada.archive.2003.0016.

Gilbert, G.H., Tilashalski, K.R., Litaker, M.S., McNeal, S.F., Boykin, M.J., Kessler, A.W., DPBRN Collaborative Group, 2010. Outcomes of root canal treatment in dental practice-based research network practices. General Dentistry 58 (1), 28–36.

Grisi, D.C., Vieira, I.V., de Almeida Lima, A.K., de Oliveira Mattos, M.C., Damé-Teixeira, N., Salles, L.P., de Oliveira, L.A., Stefani, C., do Carmo Machado Guimarães, M., 2022. The complex interrelationship between diabetes mellitus, oral diseases and general health. Curr. Diabet. Rev. 18 (3) https://doi.org/10.2174/1573399817666210322153210.

Gupta, A., Aggarwal, V., Mehta, N., Abraham, D., Singh, A., 2020. Diabetes mellitus and the healing of periapical lesions in root filled teeth: a systematic review and meta-analysis. Int. Endod. J. 53 (11), 1472–1484. https://doi.org/10.1111/iej.13366.

Inchingolo, F., Tatullo, M., Abenavoli, F.M., Marrelli, M., Inchingolo, A.D., Inchingolo, A. M., Dipalma, G., 2011 Jan. Non-Hodgkin lymphoma affecting the tongue: unusual intra-oral location. Head Neck Oncol. 4 (3), 1. https://doi.org/10.1186/1758-3284-3-1. PMID: 21205320; PMCID: PMC3022892.

Jiang, W., Liang, J.P., 2022. [Overview of technical advances in the diagnosis of pulp and periapical diseases]. Zhonghua Kou Qiang Yi Xue Za Zhi = Zhonghua Kouqiang Yixue Zazhi = Chinese Journal of Stomatology 57 (3), 227–232. https://doi.org/10.3760/cma.j.cn112144-20211111-00497.

Khalighinejad, N., Aminoshariae, M.R., Aminoshariae, A., Kulild, J.C., Mickel, A., Fouad, A.F., 2016. Association between systemic diseases and apical periodontitis. J. Endod. 42 (10), 1427–1434. https://doi.org/10.1016/j.joen.2016.07.007.

Khandelwal, A., Janani, K., Teja, K., Jose, J., Battineni, G., Riccitiello, F., Valletta, A., Palanivelu, A., Spagnuolo, G., 2022. Periapical healing following root canal treatment using different endodontic sealers: a systematic review. BioMed Res. Int. 2022, 1–9. https://doi.org/10.1155/2022/3569281.

Laukkanen, E., Vehkalahti, M.M., Kotiranta, A.K., 2019. Impact of systemic diseases and tooth-based factors on outcome of root canal treatment. Int. Endod. J. 52 (10), 1417–1426. https://doi.org/10.1111/iej.13143.

Lo Giudice, R, Machado, PS, 2023. Dal Piva AMdO, Tribst JPM. Influence of Placement of Ultrashort Implant at Sub-Crestal, Crestal and Supra-Crestal Level with Titanium or Polyetheretherketone Hybrid Abutment: 3D Finite Element Analysis. Prosthesis 5 (3), 721–732. https://doi.org/10.3390/prosthesis5030051.

López-López, J., Jané-Salas, E., Estrugo-Devesa, A., Velasco-Ortega, E., Martín-González, J., Segura-Egea, J.J., 2011. Periapical and endodontic status of type 2 diabetic patients in Catalonia, Spain: a cross-sectional study. J. Endod. 37 (5), 598–601. https://doi.org/10.1016/j.joen.2011.01.002.

Makanjuola, J, Deb, S, 2023. Chemically Activated Glass-Ionomer Cements as Bioactive Materials in Dentistry: A Review. Prosthesis 5 (1), 327–345. https://doi.org/10.3390/prosthesis5010024.

Marotta, P.S., Fontes, T.V., Armada, L., Lima, K.C., Rôças, I.N., Siqueira, J.F., 2012. Type 2 diabetes mellitus and the prevalence of apical periodontitis and endodontic treatment in an adult Brazilian population. J. Endod. 38 (3), 297–300. https://doi.org/10.1016/j.joen.2011.11.001.

Marwan, S.H., Todo, M., 2022. Effects of hysteresis on the dynamic deformation of artificial polymeric heart valve. Prosthesis 4 (4), 511–523. https://doi.org/10.3390/prosthesis4040042.

Mindiola, M.J., Mickel, A.K., Sami, C., Jones, J.J., Lalumandier, J.A., Nelson, S.S., 2006. Endodontic treatment in an american indian population: a 10-year retrospective study. J. Endod. 32 (9), 828–832. https://doi.org/10.1016/j.joen.2006.03.007.

Minervini, G., Franco, R., Marrapodi, M.M., Fiorillo, L., Cervino, G., Cicciù, M., 2023a. Prevalence of temporomandibular disorders (TMD) in pregnancy: a systematic review with meta-analysis. J. Oral Rehabil. https://doi.org/10.1111/joor.13458.

Minervini, G., Franco, R., Marrapodi, M.M., Fiorillo, L., Cervino, G., Cicciù, M., 2023b. Prevalence of temporomandibular disorders in children and adolescents evaluated with Diagnostic Criteria for Temporomandibular Disorders: a systematic review with meta-analysis. J. Oral Rehabil. 50 (6), 522–530. https://doi.org/10.1111/joor.13446.

Minervini, G., Franco, R., Marrapodi, M.M., Ronsivalle, V., Shapira, I., Cicciù, M., 2023c. Prevalence of temporomandibular disorders in subjects affected by Parkinson disease: a systematic review and metanalysis. J. Oral Rehabil. https://doi.org/10.1111/joor.13496.

Ng, Y.-L., Mann, V., Gulabivala, K., 2011. A prospective study of the factors affecting outcomes of non-surgical root canal treatment: part 2: tooth survival. Int. Endod. J. 44 (7), 610–625. https://doi.org/10.1111/j.1365-2591.2011.01873.x.

Palumbo, C., Nicolaci, N., La Manna, A.A., Branek, N., Pissano, M.N., 2018. Association between central diabetes insipidus and type 2 diabetes mellitus. Medicina 78 (2), 127–130.

Polychronakis, N, Mikeli, A, Lagouvardos, P, Polyzois, G, 2023. Effects of Disinfectants Used for COVID-19 Protection on the Color and Translucency of Acrylic Denture Teeth. Prosthesis 5 (1), 102–112. https://doi.org/10.3390/prosthesis5010009.

Romanos, GE, Schesni, A, Nentwig, G-H, Winter, A, Sader, R, Brandt, S, 2023. Impact of Implant Diameter on Success and Survival of Dental Implants: An Observational

Cohort Study. Prosthesis 5 (3), 888–897. https://doi.org/10.3390/prosthesis5030062.

Rudranaik, S., Nayak, M., Babshet, M., 2016. Periapical healing outcome following single visit endodontic treatment in patients with type 2 diabetes mellitus. J Clin Exp Dent 0–0. https://doi.org/10.4317/jced.52859.

Santos, MC, Azevedo, L, Fonseca, P, Viana, PC, Araújo, F, Villarinho, E, Fernandes, GVO, Correia, A, 2023. The Success Rate of the Adhesive Partial Fixed Prosthesis after Five Years: A Systematic Review. Prosthesis 5 (1), 282–294. https://doi.org/10.3390/prosthesis5010021.

Segura-Egea, J.J., Jimenez-Pinzon, A., Rios-Santos, J.V., Velasco-Ortega, E., Cisneros-Cabello, R., Poyato-Ferrera, M., 2005. High prevalence of apical periodontitis amongst type 2 diabetic patients. Int. Endod. J. 38 (8), 564–569. https://doi.org/10.1111/j.1365-2591.2005.00996.x.

Sisli, S.N., 2019. Evaluation of the Relationship between type ii diabetes mellitus and the prevalence of apical periodontitis in root-filled teeth using cone beam computed tomography: an observational cross-sectional study. Med. Princ. Pract. 28 (6), 533–538. https://doi.org/10.1159/000500472.

Tanaka, K., Yamaguchi, T., Kaji, H., Kanazawa, I., Sugimoto, T., 2013. Advanced glycation end products suppress osteoblastic differentiation of stromal cells by activating endoplasmic reticulum stress. Biochem. Biophys. Res. Commun. 438 (3), 463–467. https://doi.org/10.1016/j.bbrc.2013.07.126.

Trope, M., Delano, E.O., Ørstavik, D., 1999. Endodontic treatment of teeth with apical periodontitis: Single vs. Multivisit treatment. J. Endod. 25 (5), 345–350. https://doi.org/10.1016/S0099-2399(06)81169-6.

Uğur Aydın, Z., Ocak, M.G., Bayrak, S., Göller Bulut, D., Orhan, K., 2021. The effect of type 2 diabetes mellitus on changes in the fractal dimension of periapical lesion in teeth after root canal treatment: a fractal analysis study. Int. Endod. J. 54 (2), 181–189. https://doi.org/10.1111/iej.13409.

Vlassara, H., 1997. Recent progress in advanced glycation end products and diabetic complications. Diabetes 46 (Supplement_2), S19–S25. https://doi.org/10.2337/diab.46.2.S19.

Wang, T.-F., Jen, I.-A., Chou, C., Lei, Y.-P., 2014. Effects of periodontal therapy on metabolic control in patients with type 2 diabetes mellitus and periodontal disease. Medicine 93 (28), e292. https://doi.org/10.1097/MD.0000000000000292.