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Systematic Review

Prevalence of Root Canal Treatments among Diabetic Patients: Systematic Review and Meta-Analysis

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Abstract: (1) Apical periodontitis (AP) is the inflammatory response of the periapical tissue to bacterial antigens and toxins arriving from inside the root canal after pulp necrosis. To control AP, it is necessary to interrupt the passage of antigens from the root canal to the periapex, which is achieved via a root canal treatment (RCT), which is the indicated endodontic therapy in cases of AP. The prevalence of root-filled teeth (RFT) is an indicator of the frequency of endodontic infections and the degree of dental care. Diabetes is associated with AP and has been identified as the main prognostic factor in RCT. The aim of this study was to carry out a systematic review with meta-analysis answering the following question: What is the prevalence of RFT among diabetic patients? (2) This study was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines 2020. A literature search was undertaken without limits on time or language until 12 January 2023 in PubMed-MEDLINE, Embase and Scielo. All studies reporting the prevalence of RFT among diabetic patients via radiographic examination; both panoramic and periapical radiographs were included. Meta-analyses were calculated with Open Meta Analyst software. The main outcome variable was the prevalence of RFT, calculated as the total number of RFT divided by the total number of teeth, which is expressed as a percentage. As a secondary outcome variable, the prevalence of diabetic patients with at least one RFT, expressed as a percentage, was also calculated. The quality of evidence of the included studies was analyzed according to the guidelines provided by the Centre for Evidence-Based Medicine in Oxford. The risk of bias was assessed using the Newcastle–Ottawa Scale, which was adapted for cross-sectional studies. To estimate the variance and heterogeneity amongst the trials, the Higgings I2 test was employed. (3) Eight studies fulfilled the inclusion criteria. Four studies were classified as having a high risk of bias, and four were classified as having a moderate risk of bias. The prevalence of RFT was estimated for 37,922 teeth and 1532 diabetic patients. The overall calculated prevalence of RFT among diabetic patients was 5.5% (95% CI = 4.1–6.9%; $p < 0.001$). The percentage of diabetics who had at least one RFT was 42.7% (95% CI = 23.9–61.4%; $p < 0.001$). (4) This systematic review and meta-analysis concluded that the prevalence of RFT among diabetic patients is 5.5%. More than 40% of diabetics have at least one RFT. In daily clinics, dentists should suspect that patients are undiagnosed diabetics when multiple RCT failures are observed in the same patient.

Keywords: diabetes; endodontics; epidemiology; root canal treatment; root-filled teeth; prevalence; survey; population-based study

Citation: León-López, M.; Cabanillas-Balsera, D.; Martín-González, J.; Díaz-Flores, V.; Areal-Quecuty, V.; Crespo-Gallardo, I.; Montero-Miralles, P.; Segura-Egea, J.J. Prevalence of Root Canal Treatments among Diabetic Patients: Systematic Review and Meta-Analysis. *Appl. Sci.* **2023**, *13*, 5957. https://doi.org/10.3390/app13105957

Academic Editor: Irene Graça Azevedo Pina-Vaz

Received: 13 April 2023
Revised: 27 April 2023
Accepted: 11 May 2023
Published: 12 May 2023

1. Introduction

When bacteria, their toxins or their antigens reach the dental pulp, the pulpal inflammatory reaction, pulpitis, ends up inducing pulp necrosis [1]. If an adequate treatment is

not instituted, toxins and antigens will pass through the apical foramen into the periapical tissues, inducing the immune and inflammatory reaction characteristic of apical periodontitis (AP) [2]. To control AP, it is necessary to interrupt the passage of antigens from the root canal to the periapex, which is achieved via a root canal treatment (RCT) [3]. RCTs are focused on eliminating bacteria that cause an infection in the root canal system using chemical and mechanical methods [4]. Both AP and RCT are highly prevalent, with at least one tooth affected by AP in 52% of people [5], and 8% of the teeth of the world population being root-filled teeth (RFT) [6].

On the other hand, several epidemiological studies on endodontic medicine have reported the high prevalence of AP among patients affected by some systemic diseases [7–10]. In the specific case of diabetes, there are many cross-sectional and case–control epidemiological studies that have found a higher prevalence of AP among diabetic patients [11–16]. Diabetes mellitus is characterized by an inadequate carbohydrate, lipidic and protein metabolism; its primary aspect is hyperglycemia [17,18]. Hyperglycemia acts as the main cause of the incidence and progression of microvascular complications associated with the disease (retinopathy, nephropathy and neuropathy). Two main types of diabetes have been established: type 1 diabetes (insulin-dependent diabetes) is characterized by deficient production of insulin by the pancreas and requires external administration of this hormone; type 2 diabetes (non-insulin dependent diabetes) is characterized by the ineffective use of insulin by the cells of the body, representing 95% of all diabetics [19,20].

Given the high prevalence of AP among diabetic patients [11,13,15,16,21,22], it can be expected that the prevalence of RFT is also high among those patients. However, several systematic reviews have concluded that diabetes is a major preoperative prognostic factor in root canal therapy [23–25], negatively influencing the treatment outcome and RFT survival rate [26,27]. Therefore, diabetics could have a lower prevalence of RFT than the general population does. On the other hand, diabetic patients have a high prevalence of periodontal disease [28,29], which also leads them to lose a greater number of teeth than the healthy non-diabetic population does [30].

The aim of this study was to conduct a systematic review and meta-analysis investigating the prevalence of RFT among diabetic patients.

2. Materials and Methods

This study was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines 2021 [31] and the methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and cumulative incidence data [32]. The CoCoPop mnemonic has been followed to formulate the review question [32], as follows: What is the prevalence of RFT (Co, condition) among diabetic patients (Pop, population) around the world (Co, context)?

The main outcome was the percentage of RFT. As a secondary outcome, we took into account the percentage of people with at least one RFT.

2.1. Literature Search Strategy

A literature search was undertaken without limits on time or language until 12 January 2023 in PubMed-MEDLINE, Embase and Scielo. The most frequently cited descriptors in the previous publication on this theme were used in the electronic search strategy using combining Medical Subject Heading (MeSH) terms and text words (tw). The search strategy is shown in Box 1.

Box 1. Key words and search strategy.

(Diabetes OR Diabetes Mellitus OR Hyperglycemia OR Diabetic) AND (nonvital tooth OR nonvital tooth OR tooth nonvital OR tooth nonvital OR nonvital teeth OR teeth nonvital OR devitalized tooth OR tooth devitalized OR devitalized teeth OR teeth devitalized OR pulpless tooth OR tooth pulpless OR pulpless teeth OR teeth pulpless OR endodontically-treated teeth OR teeth endodontically-treated OR endodontically-treated tooth OR tooth endodontically-treated) AND (cross-sectional studies OR cross-sectional OR cross-sectional design OR cross-sectional research OR prevalence studies OR prevalence study OR survey OR prevalence OR epidemiologic studies OR epidemiologic study OR cohort studies OR cohort study OR concurrent studies OR concurrent study OR incidence studies OR incidence study OR case-control studies OR case-control study)

Complementary screening was performed to look for any additional studies among the references of the included studies.

2.2. Eligibility Criteria

The studies that have been included are all those that provided information on the frequency of endodontic teeth among diabetic patients, as determined by radiographic examination.

The following exclusion criteria were applied: studies that evaluated the prevalence of RFT only among non-diabetic patients, those that did not report data on the prevalence of RFT, those that did not provide full mouth information, those that included patients with mixed dentition, and those that did not contrast their findings with radiographic examination, as well as reviews, letters, posters, conference proceedings or case series, and dissertations

2.3. Study Selection

The studies were selected by three of the authors (D.C.-B., M.L.-L., and J.J.S.-E.) by evaluating titles and abstracts. The full text was accessed when the title and abstract did not allow the authors to judge the study. Next, full texts were analyzed and the articles that met the eligibility criteria were selected. In case of disagreement, it was resolved by the three authors reaching a consensus.

2.4. Data Collection/Extraction Process

The same authors collected information about the selected studies. For each article, the following information was extracted: authors, year of publication, participants, radiographs used, the number of teeth, the number of RFT and the number of people with at least one RFT.

2.5. Quality Assessment and Risk of Bias of Individual Studies

The guidelines provided by the Centre for Evidence-Based Medicine in Oxford [33] were used to analyze the quality of evidence in the included studies. The risk of bias was assessed using the Newcastle–Ottawa Scale, which was adapted for cross-sectional studies [6,34].

Three authors (D.C.-B., M.L.-L., and J.M.-G.) independently assessed the risk of bias of each of the included studies. In case of disagreement, the authors discussed it until they reached an agreement.

Two domains were taken into account when analyzing the quality assessment and risk of bias of the individual studies: sample selection and outcome. The domain sample selection included the following items: the representativeness of the sample, sample size and non-respondents. The domain outcome included the following items: the assessment of the outcome, the inclusion of third molar in the outcome, the inclusion of edentulous in total sample and the number of observers. The evaluation of each item was conducted according to the criteria previously described [6]. The maximum possible score was 12 points. A high risk of bias was defined as from 0 to 4 points, a moderate risk of bias was considered for the studies scoring from 5 to 8 points, and finally, a low risk of bias was assigned to studies scoring between 9 and 12 points.

In studies whose sample included edentulous patients, only dentate patients were considered for statistical analysis.

2.6. Outcome of Interest

The main outcome variable was the prevalence of RFT, which was expressed as a percentage. As a secondary outcome variable, the prevalence of diabetic patients with at least one RFT, expressed as a percentage, was also calculated.

2.7. Data Synthesis and Statistical Analysis

The prevalence of RFT among diabetic patients was calculated by carrying out a meta-analysis using OpenMeta Analyst version 10.10 software [35] using the binary random effects model. Another meta-analysis was performed also using subgroup based on the number of total diabetic population with at least one RFT. Higgings I^2 test was employed to estimate the variance and heterogeneity amongst the trials. A slight degree of heterogeneity was considered when I^2 was 25–50%, a moderate degree was considered when it was between 50 and 75%, and a high degree was considered when it was >75% [36].

3. Results

3.1. Selection of the Studies

Figure 1 shows the flow diagram of the search strategy, according to PRISMA 2020 instructions. After the initial search, 26 published studies were selected. There were no duplicate studies. After examining the titles and abstracts, 15 of the 26 eligible papers, those that did not investigate RFT, were excluded. Before, the full text of the remaining 11 studies were comprehensively read. Three studies were excluded: one was included because it only included RFT [37], and two others were included because they did not provide data on RFT [38,39]. Finally, eight studies were selected for the systematic review and meta-analysis [11,13–16,21,40,41].

3.2. Characteristics of the Included Studies

Table 1 shows the main features of the included studies [11,13–16,21,40,41]: sample size, age and sex distribution, type of diabetes suffered by the patients, radiographs used and the prevalence of RFT. Seven of them also provided data on the percentage of diabetic people with at least one RFT [11,13–15,21,40,41].

3.3. Outcome of the Primary Meta-Analysis and Publication Bias

The eight studies added a total of 1532 people who had 37,922 teeth in total, of which 2156 were RFT [11,13–16,21,40,41]. Figure 2 shows the forest plot of the primary meta-analysis. The overall calculated prevalence of RFT among diabetic patients was 5.5% (95% CI = 4.1–6.9%; $p < 0.001$). The heterogeneity value was $I^2 = 96\%$.

Another analysis was carried out including the seven studies, providing information about patients with at least one RFT (Figure 3) [11,13–15,21,40,41]. This meta-analysis included a total of 1387 patients, of which 203 had at least one RFT (42.7%; 95% CI = 23.9–61.4%; $p < 0.001$). The heterogeneity value was $I^2 = 98\%$.

3.4. Quality Assessment and Risk of Bias

Quality assessment and risk of bias was evaluated for each study (Table 2). According to the guidelines provided by the Centre for Evidence-Based Medicine in Oxford [33], all the studies were classified as level 4. Four out of eight studies were classified as having a high risk of bias [11,15,21,41], and four of them were classified as having a moderate risk of bias [13,14,16,40]. None of the included studies were classified as having a low risk of bias.

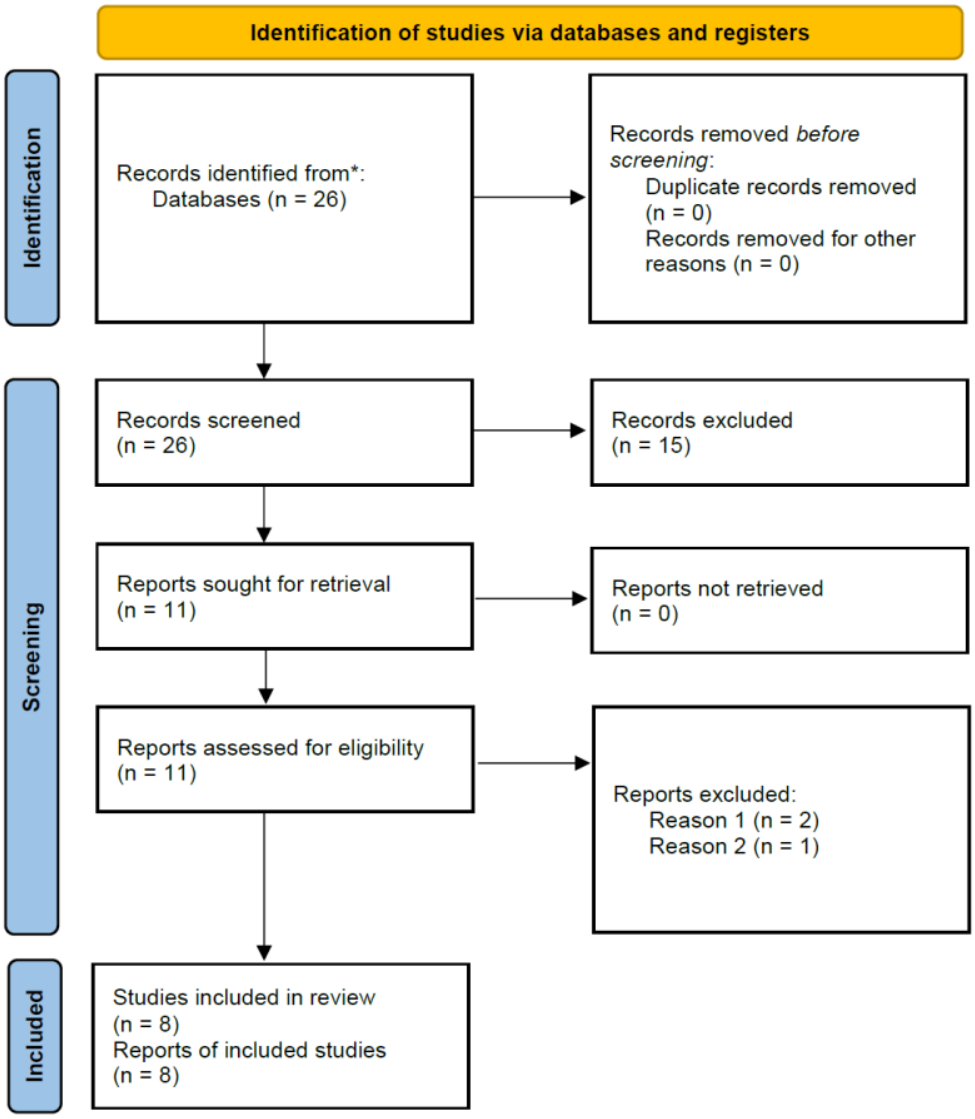

Figure 1. Flow diagram of the search strategy of the systematic review and meta-analysis following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines 2020 [31].

Table 1. Characteristics of the included studies, main outcomes and type of evidence.

Authors	Year	Study Design	Sample Size	No of Teeth	Gender (%)	Age	Radiographs	No. of RFT	Prevalence of RFT (%)	People with at Least One RFT (%)	Type of Evidence [33]
Segura-Egea et al. [21]	2005	Cross-sectional	32 type 2	692	12 men; 20 women	43–74	Periapical (1 observer)	12	2	31	4
López-López et al. [11]	2011	Cross-sectional	50 type 2	1095	20 men; 30 women	44–83	Panoramic	85	7.8	70	4
Marotta et al. [15]	2012	Cross-sectional	30 type 2	652	12 men; 18 women	40–69	Periapical + Panoramic (2 observers)	85	13	76.7	4
Sánchez-Domínguez et al. [14]	2015	Cross-sectional	83 type 2	1751	49 men; 51 women	66.6 ± 10.6	Panoramic (3 observers)	58	3.3	32.5	4
Al-Nazhan et al. [40]	2017	Cross-sectional	926	25,028	540 men; 386 women	>18	Panoramic (2 observers)	1541	6.16	4.6	4
Smadi [16]	2017	Cross-sectional	145 type 2	3111	71 men; 74 women	Not provided	Panoramic (2 observers)	130	4.18	Not provided	4
Pérez-Losada et al. [13]	2020	Cross-sectional	216 type 2	4514	117 men; 99 women	Not provided	Panoramic (3 observers)	173	3.8	12.5	4
Limeira et al. [41]	2020	Cross-sectional	50 type 2	1079	23 men; 27 women	18–45	Panoramic (1 observer)	72	6.7	76	4

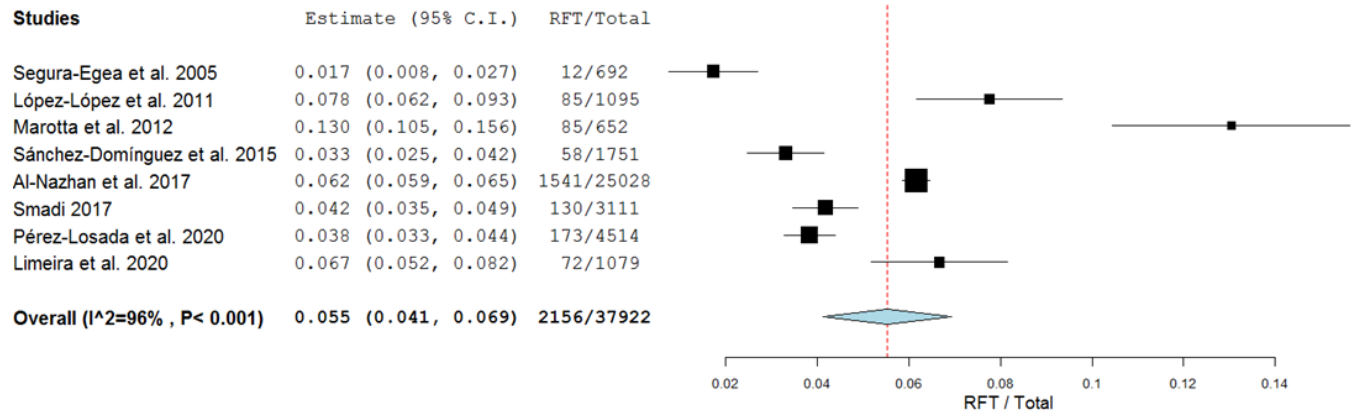

Figure 2. Forest plot of the primary meta-analysis showing the prevalence of RFT in the diabetic adult population [11,13–16,21,40,41].

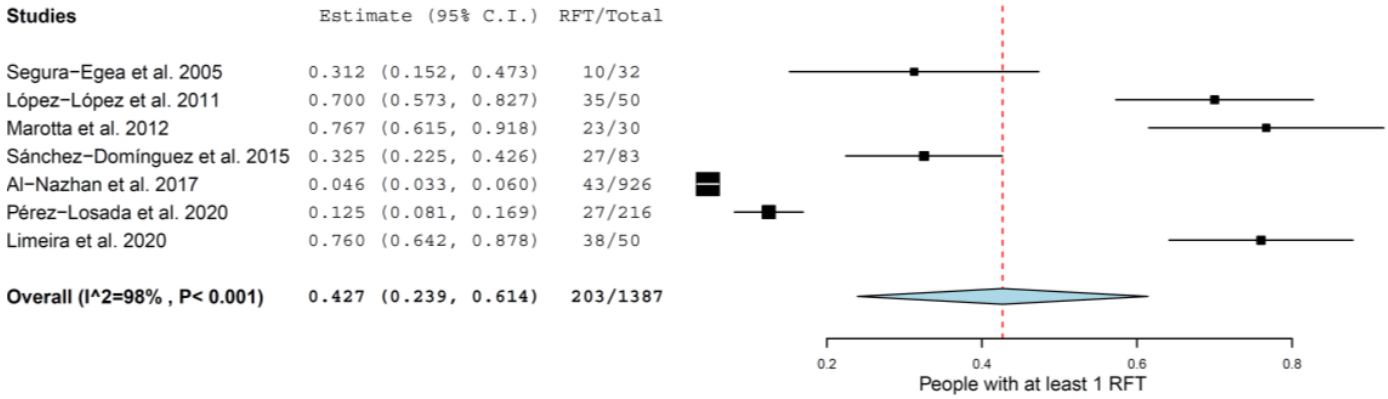

Figure 3. Forest plot of the studies that have calculated the percentage of people with at least one RFT in the total sample [11,13–15,21,40,41].

Table 2. Quality assessment and risk of bias of individual studies according to the criteria previously described [6]: High risk of bias was defined as from 0 to 4 points, a moderate risk of bias was considered for the studies scoring from 5 to 8 points, and finally, a low risk of bias was assigned to studies scoring between 9 and 12 points. Each * is one point.

Authors	Year	Study Design	Selection			Outcome			Risk of Bias
			Representativeness of the Sample	Sample Size Calculation	Non-Respondents	Asse-ssment	Inclusion of Third Molar	Inclusion of Eden-tulous in Sample	No. of Observers	
Segura-Egea et al. [21]	2005	Cross-sectional	*			**	*			High
López-López et al. [11]	2011	Cross-sectional	*			*	*		*	High
Marotta et al. [15]	2012	Cross-sectional	*			**			*	High
Sánchez-Domínguez et al. [14]	2015	Cross-sectional	*			**	*	**	*	Moderate
Al-Nazhan et al. [40]	2017	Cross-sectional	**			*	*	**	*	Moderate
Smadi [16]	2017	Cross-sectional	*		*	**			*	Moderate
Pérez-Losada et al. [13]	2020	Cross-sectional	*			**	*	**	*	Moderate
Limeira et al. [41]	2020	Cross-sectional	*			*	*		*	High

4. Discussion

The aim of this study was to conduct a systematic review to determine the prevalence of RFT among the diabetic adult population. According to the raw data from the primary study, it can be concluded that the prevalence of RFT among the diabetic adult population over 18 years is 5.5%, with 42.7% of diabetic people having one or more RFT. The systematic review and meta-analysis of prevalence and incidence are emergent methodologies in the field of evidence synthesis. The traditionally used PICO strategy does not agree with prevalence studies, so the CoCoPop rule was used [32].

Taking into account the worldwide prevalence of RFT (8.3% of teeth and 55.7% of people) [6], the results of this study show a strikingly lower prevalence of RFT among diabetics compared to that of the general population. Moreover, the prevalence of RFT is an indicator of the frequency of endodontic infections and, at least apparently, these results are not consistent with the higher prevalence of AP among diabetic patients that has been shown [13–15,21,22,38]. On the contrary, an increase in the prevalence of RCT could be expected among the adult diabetic population. However, the explanation for the lower prevalence of RFT among diabetics probably lies in the fact that diabetic patients suffer from post-treatment AP more frequently [24,42], which is possibly consecutive to a delay in the healing of periapical tissues [43,44]. The persistence of AP among diabetics after RCT leads, in some cases, to tooth extraction. In fact, type 2 diabetes is associated with greater loss of RFT [23], and most of the studies included in the present study [11,13–16,21] refer to type 2 diabetics. However, since it is not possible to learn about the quality of RCT or other possible prognostic factors, no definitive conclusions can be drawn in this regard.

Diabetes mellitus includes a group of disorders of the metabolism of carbohydrates, lipids and proteins, the main manifestation of which is hyperglycemia, as a result of a deficiency in insulin secretion, a lack of insulin action, or both [19]. Chronic hyperglycemia is associated with glucotoxicity and the damage and dysfunction of various organs, especially the eyes, kidneys, nerves, heart and blood vessels [19,20]. The results of several studies support a relationship between the prevalence of AP and diabetes [7,11,15,16,21,22,39]. Furthermore, several systematic reviews and meta-analyses have found a significant association between the endodontic treatment outcome and diabetes [23,24,26]. On the other hand, several studies have found a correlation between the higher prevalence of AP and poor glycemic control among diabetic patients [13,14,16]. In short, there seems to be a mutual influence between diabetes and AP [7,45].

The pro-inflammatory state and impaired immune response associated with diabetes may affect the reparative response of the periapical tissue, influencing the two main endodontic variables: the prevalence of AP and the frequency of RCT [46]. Innate immunity is the first line of defense against pathogens. Systemic conditions that alter the functions of innate immunity cells, such as diabetes, decrease neutrophil phagocytosis or macrophage chemotaxis, causing an inflammatory state that alters cell proliferation, delaying lesion healing. Especially in poorly controlled diabetic patients, a stronger systemic inflammatory reaction may be induced, with the activation of NF-κβ in macrophages and increased cellular oxidative stress, which may impair bone turnover and periapical wound healing [47]. These clinical situations are characterized by increased C-reactive protein levels in serum and the release of potentially tissue-destructive substances, such as reactive oxygen species, collagenase, serine proteases and the up-regulation of pro-inflammatory cytokines (IL-1b, IL-6, IL-8, IL-10 and TNF-α) [7]. All these biological changes result in further progression of the periapical inflammation and impaired periapical healing, ending with the loss of the RFT [45].

The outcome of RCT among diabetic subjects and controls has been prospectively investigated [48,49]. The rate of periapical healing was significantly lower in the diabetic group (43%) compared to that in the non-diabetic group (80%) ($p < 0.05$) after a 12-month follow-up [49]. In another study, the clinical and radiographic cure results of a RCT performed in a single visit on patients with type 2 diabetes mellitus with PA were evaluated, concluding that type 2 diabetics had larger chronic lesions compared to those of the control

subjects, with there being slower and delayed clinical and radiographic healing among diabetic patients [48].

A recent umbrella review concluded that diabetes is a risk factor for the outcome of RCT [26]. Diabetes can be considered as a key preoperative prognostic factor in endodontic treatment [26,45]. In short, the greater rate of the loss of endodontically treated teeth could explain the low prevalence of RCT among diabetic patients compared with that of the general population [6].

On the other hand, a possible explanation for the lower prevalence of RFT among diabetics is also periodontal disease. Diabetic patients have a high prevalence of periodontal disease [28]. Diabetes and periodontal disease are closely linked and amplify one another, if they are not successfully controlled [50]. Considering that periodontal disease is also a leading cause of tooth loss [51], the low prevalence of RFT among diabetics could also be explained by the loss of endodontically treated teeth caused by periodontal disease. The combined effect of diabetes itself and periodontal disease can reasonably explain the low prevalence of RFT among diabetics.

Finally, another possible explanation that should also be taken into account is the increase in the number of dental implant treatments that has occurred in the last three decades [52]. Dentists and diabetic patients might prefer the extraction of teeth affected by endodontic infections and their replacement by dental implants, instead of performing RCT.

Regarding the articles included in the systematic review, the initial database search provided twenty-six articles. When the inclusion criteria were applied, it resulted in a systematic review of eight studies published in the first quarter of the 21st century. All the included studies were cross-sectional studies investigating both the prevalence of AP and RCT among diabetic patients. Most of the studies [11,13,14,16,40,41] used panoramic radiographs to detect RFT, another [21] used periapical radiographs and another one [15] used both periapical and panoramic radiographs. Although it might be thought that the detection of RFT can be performed with the same precision with panoramic and periapical radiographs, in previous studies, the prevalence of RFT has been found to be higher with the use of periapical radiographs [6].

The results of this study should be translated to the clinical practice [53]. As we have collected data on poor healing and the tendency to tooth extraction among diabetic patients, it is important to bear in mind that the prognosis of RCT can be poor among diabetic patients. However, this should not be an excuse for not focusing all the attention on making a good quality RCT. In addition, this can help dentists suspect undiagnosed diabetic patients when they recognize numerous failures of RCT. If in doubt, the patient should be referred for blood tests and additional tests to rule out diabetes.

Some limitations of this systematic review should be noted. One important limitation is the low numbers of included studies and patients. The reason lies in the fact that a few studies followed a strict protocol for the selection of the individuals included in the sample. This is also the reason why none of the studies included in this systematic review and meta-analysis had a low risk of bias. Thus, the results of this systematic review must be carefully assessed taking into account the quality of the included studies. Four of the included studies were classified as having a high risk of bias [11,15,21,41], while the other four studies were classified as having a moderate risk of bias [13,14,16,40]. None of the included studies calculated the sample size, which is necessary to ensure a correct sample size to justify the study results. Moreover, more than a half of the studies did not mention if edentulous patients were included in the sample, which alters the results of meta-analyses [11,15,16,21,41]. Only one [40] of the included studies had a reasonable representativeness of the sample, but none of them used the random sampling method. Given the very low proportion of RCT performed on third molars, whether or not the third molar was included in the study does not represent a major limitation. So, a low risk of bias was considered if the third molar was not included in the total patient sample. Similarly, if edentulous patients were not included in the total patient sample, a low risk of bias was also considered. Nevertheless, when the study did not specify whether it included

edentulous patients in the total sample, it was considered to having a very high risk of bias. Lastly, the total number of diabetic patients included in this review, almost 1500, is too low to reach a strong conclusion. Moreover, the heterogeneity of the studies was greater than 95%, which indicates that the differences in the design, samples and characteristics of the population are high, and this can lead to very different results, compromising the results of the meta-analysis.

5. Conclusions

This systematic review and meta-analysis concluded that the prevalence of RFT among diabetic patients is 5.5%. More than 40% of diabetics have at least one RFT. In daily clinics, dentists should suspect that patients are an undiagnosed diabetics when multiple RCT failures are observed in the same patient. A blood test that assesses blood glucose can help to rule out the presence of diabetes.

Author Contributions: Conceptualization, M.L.-L., D.C.-B. and J.J.S.-E.; formal analysis, V.D.-F. and I.C.-G.; investigation, M.L.-L. and V.A.-Q.; methodology, D.C.-B. and P.M.-M.; resources, M.L.-L. and I.C.-G.; validation, J.M.-G.; visualization, V.A.-Q.; writing—original draft, M.L.-L., V.D.-F. and P.M.-M.; writing—review and editing, J.M.-G. and J.J.S.-E. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The authors will make the study data available to the interested party upon request.

Acknowledgments: María Léon López was research fellow supported by Spanish Ministerio de Educación y Formación Profesional (collaboration grant 2020-21).

Conflicts of Interest: The authors declare no conflict of interest.

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