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Research Article

Association between Diabetes Mellitus and Extraction of Root Filled Tooth: A Systematic Review

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Abstract

Objectives: Diabetes mellitus is one of the most prevalent diseases worldwide. It is associated with decreased quality of life, high infection rate, and decreased wound healing. This leads to many complications especially, for endodontics. That is why in this study, we will assess the effect of diabetes on the root canal therapy for the apical periodontitis.

Methods: Four databases were searched using specific search terms. We included assess the risk of failure of root canal therapy in diabetic patients and the prevalence of root canal therapy failure and different outcomes reported in diabetic patients. The studies were assessed for the quality of evidence using the NIH quality assessment tool before being included for the review.

Results: Six studies fulfilled our inclusion criteria and had passed the quality assessment to be included for the qualitative evidence synthesis. Based on these studies, diabetes mellitus had the worst outcome among other systemic diseases. Two studies assessed factors affecting the outcome and it was related to preoperative preparation and state of the necrotic teeth. However, it was not significantly correlated with the HBA1C level.

Conclusion: Diabetes did not cause the failure of the root canal treatment but caused delayed healing. Diabetes effect on the root canal therapy is dependent on many factors that need to be more assessed in more studies.

Keywords: *Apical Periodontitis; Root Canal Therapy; Diabetes Mellitus; Endodontic Treatment; Endodontics*

Introduction

Diabetes mellitus is considered a major global threat due to its high rate of morbidities and complications [1]. It is estimated that every one of eleven adults is diagnosed with Diabetes. In 2040, it is estimated that Diabetes Mellitus will affect 642 million patients [1,2]. Type II Diabetes Mellitus is considered the most common type affecting 90% of diabetic patients [2]. The onset of Type II Diabetes starts

on adulthood aging 20 - 79 years estimated to be diagnosed in 415 million adults [3]. The global burden of type II diabetes is increasing every year ranked as the ninth cause of decreased quality of life. Moreover, diabetic complications were responsible for 6.8% mortality worldwide. Moreover, the disability risk in type II diabetes has increased in recent years, occupying the third cause in 2015 after it was fourth in 2005 [1,2,4].

One of the most common morbidities associated with diabetes is infection [2,5]. Infection-related mortality in diabetic patients has been investigated in recent years [6]. A study reported that diabetes increased infection-related mortality two times and a half compared to healthy controls [7]. Bertoni., *et al*. followed 9000 patients for 12 - 16 years and found that diabetes increased the infection-related mortality mainly because accompanying microvascular and macrovascular complications not due to glucose metabolism itself [6]. Diabetes Mellitus also increased the susceptibility to infection as evidenced by many studies [6-9]. A study found that there was an increased risk of bacterial infection, and patients were more prone to rare types of infections [6-9]. Moreover, patients were more prone to rare complications from common bacterial infections. The increased susceptibility to infection is mainly related to the influence of diabetes on the inflammatory and immune response of the patients. There is a dysfunction of leucocytes, an increase in the pro-inflammatory cytokines, and increased glycation end products resulted in increased tissue oxidation and oxidative stress [10]. Furthermore, diabetic patients usually develop post-surgical complications due to infections and impaired wound healing that is caused by dysfunction of growth factors [2,7-9].

One of the most persistent infections in diabetic patients is apical periodontitis [11]. The apical periodontitis is an inflammatory condition that affects the root system of the teeth [12]. It is considered the most prevalent teeth condition in the world affecting 34 - 61% of the population and it is more common in older age [12,13]. It is caused by microbial infection of the root system of the teeth that live in the necrotic pulp forming a biofilm of microorganisms embedded in the exopolysaccharide matrix [12,13]. The fluid part of the canal is usually infected with planktonic microorganisms [12,13]. The treatment of apical periodontitis is mainly directed through root canal therapy [14]. It is consisted of eradicating the infection and root canal filling to avoid reinfection. Usually, the treatment is successful in about 90% of cases, however, this is not the case for diabetic patients [13,14]. There is a high prevalence of persistent apical periodontitis in diabetic patients [15-18]. It is usually related to persistent infection and decreased wound healing resulting in the failure of the root canal therapy. A meta-analysis confirmed that there is an increased failure of root canal therapy in these patients due to delayed repair and persistent infections that will results ultimately in the loss of the teeth [17].

In this review, we reviewed the literature to assess the prevalence of failure of root canal therapy in diabetic patients and to report the most common mechanism of failure of root canal therapy. Moreover, we will assess the most common outcomes of root canal therapy in diabetic patients.

Methods

Database search

A comprehensive search approach was used to identify randomized controlled trials from four databases PubMed, Google Scholar, SCOPUS, and ISI web of science. The keywords used were (Apical periodontitis OR Periodontitis) AND (Diabetes OR Diabetes Mellitus OR Hyperglycaemia) AND (Endodontic OR Endodontics OR Endodontic Treatment OR Root Canal Treatment OR Root Canal Preparation OR Root Canal Therapy OR Root Filled Teeth OR Endodontically Treated Teeth). We restricted our search to human studies. All types of study designs were included.

Inclusion and exclusion criteria for screening

Specific inclusion criteria were used to identify high quality and studies that fulfill the goals of this study. Inclusion criteria are i) Studies assess the risk of failure of root canal therapy in diabetic patients, ii) Studies assess the prevalence of root canal therapy failure, and

different outcomes reported in diabetic patients. iii) Studies report the causes of the failure of root canal therapy in diabetic patients. We excluded any studies that did not compare diabetic patients to healthy groups. Experimental or animal studies were not included in this review. Books, review articles, letters to the editor, editorial reports, case reports, and conference abstracts and duplicates were excluded.

Screening for studies

The retrieved studies from each database were screened based on inclusion and exclusion criteria. First, Title/abstract screening was conducted by three independent reviewers. The included studies were then screened thoroughly to make sure it fulfills the target of this review. Each study was reviewed thoroughly to extract and build a qualitative review.

Quality assessment of the included papers

The quality of the included studies was evaluated by three reviewers using the NIH quality assessment tool that has 13 domains assessing the quality of evidence in different study designs including the cohort studies. Table 1 illustrates the 13 domains and possible answers. Two reviewers assessed the quality of each study and any disagreement were solved through discussion with the third reviewer.

Domains	Yes	No	Other (CD, NR, NA)
1. Was the research question or objective in this paper clearly stated?			
2. Was the study population clearly specified and defined?			
3. Was the participation rate of eligible persons at least 50%?			
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?			
5. Was a sample size justification, power description, or variance and effect estimates provided?			
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?			
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?			
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?			
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
10. Was the exposure(s) assessed more than once over time?			
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
12. Were the outcome assessors blinded to the exposure status of participants?			
13. Was loss to follow-up after baseline 20% or less?			
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?			

Results and Discussion

Search results

The research yielded 1664 studies that corresponded to our search terms. 675 duplicate studies were removed. Screening of the studies resulted in only six studies fulfilled the inclusion criteria and were included in the qualitative synthesis figure 1.

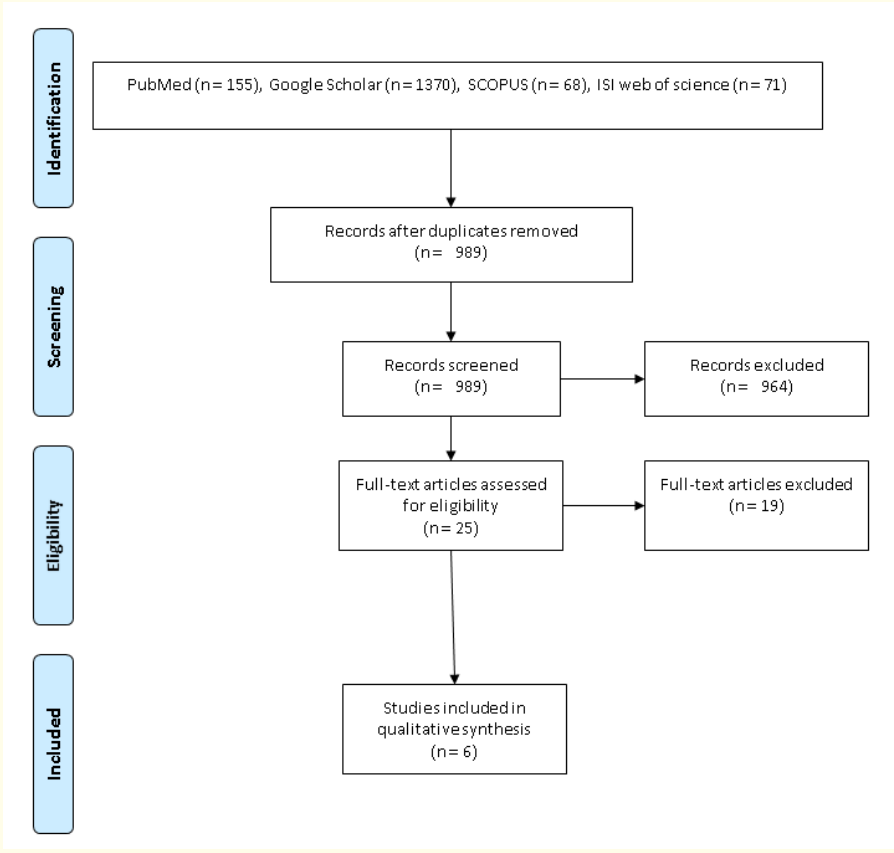

Figure 1: *PRISMA flowchart summarizing the search process in this study.*

Quality of the included studied

The included studies are considered to have high quality. Most studies had fulfilled most domains. All studies did not report the loss to follow-up. Also, only two studies were specific to diabetes mellitus, others included populations having different systemic diseases in table 2.

Patients characteristics

The study included 4708 diabetic patients who had root canal therapy. Two studies had two groups diabetic versus non-diabetic while other studies compared a group of patients who had systemic diseases including diabetic patients versus the control group. All studies are

cohort studies except Fouad., et al. who extracted the data from electronic database records. Most studies assessed the molar teeth root canal treatment outcome in table 3. Each study has assessed the outcome differently in table 3.

ID	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Laukkanen/2019 [19]	Yes	Yes	Yes	No	No	No	Yes	No	Yes	Yes	Yes	No	NA	No
Arya/2017 [15]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes
Ng/2011 [21]	Yes	Yes	Yes	No	No	No	Yes	No	Yes	Yes	Yes	No	NA	No
Wang/2011 [22]	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	NA	No
Mindiola/2006 [20]	Yes	Yes	Yes	No	No	No	Yes	No	Yes	Yes	Yes	No	NA	No
Fouad/2003 [16]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes
1. Was the research question or objective in this paper clearly stated?														
2. Was the study population clearly specified and defined?														
3. Was the participation rate of eligible persons at least 50%?														
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?														
5. Was a sample size justification, power description, or variance and effect estimates provided?														
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?														
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?														
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?														
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12. Were the outcome assessors blinded to the exposure status of participants?														
13. Was loss to follow-up after baseline 20% or less?														
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?														

Table 2: *The NIH quality assessment results.*

Study	Country	Type of study	Mean age	Diabetic patients (N)	Type of teeth	Outcome
Lauk-kanen/2019 [19]	Finland	Prospective cohort for three years	51.5	41	Molar and non-molar	Outcome was recorded as follows: 1. Healthy: Healthy periapical tissues (PAI score 1– 2). 2. Healing: Apical radiolucency considerably smaller in follow-up radiograph than in preoperative radiograph. 3. No healing: 1. Periapical radiolucency remained the same (PAI score 3–5). 2. Teeth extracted for endodontic reasons (persisting apical infection, fistula) or for reasons not recorded in documents available after root filling. 3. Teeth receiving periapical surgery. 4. Periapical radiolucency not completely disappeared after 4 years. 4. Deteriorated: Periapical radiolucency enlarged or a new periapical radiolucency emerged (PAI score 3–5)
Arya/2017 [15]	India	Prospective cohort for one year	42	21	Molar	The change in apical bone density as determined by the periapical index
Ng/2011 [21]	United Kingdom	Prospective cohort for four years	NA	22	All teeth	Tooth survival
Wang/2011 [22]	Taiwan	Prospective cohort for two years	48.6	4358	All teeth	Tooth extraction
Mindiola/2006 [20]	United States	Retrospective co-hort for ten years	Range (35 - 44)	24	All teeth	The retention of endodontically treated teeth
Fouad/2003 [16]	United States	Cross-sectional study	Younger than 40, 40 to 60, older than 60	242	All teeth	Predefined outcome categories

Table 3: *Patients characteristics in the included studies.*

The influence of diabetes on the outcome of root canal therapy of Apical periodontitis

Only two studies assessed the outcome in diabetic patients; they also assessed different factors affecting the outcome in diabetic patients [15,16]. Unlike other studies that assessed the outcome in many systemic diseases [18-21].

Fouad., *et al*. reported that diabetes only affected the healing process if there is associated pathology in the surrounding teeth. Older age, the absence of preoperative lesions, the presence of permanent restorations, and longer postoperative evaluation periods were associated with better outcomes in diabetic patients [16].

Arya., *et al*. supported the previous results diabetic patient have slower healing potential compared to non-diabetics (43% to 80%). However, all the cases recovered elucidating that diabetes did not stop the healing process rather than delaying it. In this study, they also compared the rate of healing to different levels of HBA1C, however, they did not find any significant difference between the low and high levels of HBA1C. In other words, controlling the glycemic state did not affect the healing state. This will give an insight that the effect of diabetes on the root canal therapy is not related to the glycemic state. The most important conclusion was that the treatment was delayed but it healed in diabetics even in poorly controlled cases [15].

The remaining studies investigated the effect of systemic disease on the outcome of root canal therapy. Laukkanen., *et al*. compared the outcome of root canal therapy between healthy controls and systemic diseases including diabetics. The success rate was the least in diabetic patients (73.2% compared to 85.8 of healthy control) [19]. However, this effect was more pronounced in cases with apical periodontitis preoperative than other conditions. They found that pre-existing dental pathology would affect outcome in diabetic patients as the risk of failure and extraction would be higher. Besides, when they adjusted the outcome based on the quality of root filling, type of restoration and level of alveolar bone loss are the real factors affecting the outcome irrespective of the diabetic state. Moreover, diabetes does not stop the healing process but delays it. Based on the results of this study, the preoperative condition and the condition of the alveolar bone loss are the main determining factor for the outcome of root canal therapy in diabetic patients. They also found that tooth extraction occurs in diabetics patients in case of severe alveolar bone loss. Moreover, the non-molar tooth had better results after six months (78.3 vs 88.7% molar). The indirect type of restoration also had a higher success rate within six months in diabetic patients [19].

Ng., *et al*. found that teeth survival was affected in diabetic patients and had a significantly higher rate of teeth extraction than controls. However, they found that a higher rate is not related to periodontitis. In this study, they discovered that it had higher rates of tooth extraction due to pain which is explained by neuropathy. Unlike the previous study, the type of teeth did not significantly affect the outcome of the treatment. Maxillary premolars and mandibular molars were the most frequent teeth that have teeth failure [21].

Wang., *et al*. and Mindiola., *et al*. findings supported the previous findings. They found that the risk of tooth extraction was the highest in diabetic patients.

How types of teeth affect the outcome in diabetic patients?

All studies investigated the outcome on all types of teeth except Arya., *et al*. Two studies found the outcome were similar in all teeth irrespective of its type [16,21]. In contrast, other studies reported that it was significantly affected by the type of teeth; premolars and molars had a higher risk than anterior teeth [18,20]. Ng., *et al*. elucidated that the type of teeth did not make any difference, however, it was the site of teeth that affected the outcome. The teeth that are more involved in the chewing process are more prone to extraction as evident by the higher frequency of the maxillary premolars and mandibular molars [21].

Factors affecting the rate of extraction of root filled tooth

Only two studies assessed the factors affecting the extraction of root filled teeth in diabetic patients. HbA1C levels were investigated as the cause of delayed healing, however, Arya., *et al*. found that the rate of healing and survival of the tooth was not dependent on HbA1C levels nor the control of glucose level. It was similar in non-controlled and controlled diabetic patients [15]. Fouad., *et al*. compared the prevalence of the preoperative dental pathology that may affect the outcome of root filled teeth. It was found that Type I and type II diabetes had the preoperative gingivitis, generalized probing, furcation and isolated probing [16]. They also found that extraction of root filled teeth increased significantly in cases with preoperative periradicular lesions. Surprisingly, they found that treating physicians were one of the determining factors for the success of root filled teeth survival. They found that post graduate students had less failure rates than predoctoral students. In addition, follow-up time and the length of time from final obturation to the last follow-up examination was an important determining factor for the success rate. Gender of the patients, type of teeth and preoperative sinus did not affect the outcome of root filled teeth [16]. Conclusively, Fouad., *et al*. found that younger treating physicians, less neuropathological pathogenesis, older age,

the absence of preoperative lesions, the presence of permanent restorations, and longer postoperative evaluation periods are the main determining factor for the success rate of the root filled tooth. Other reported causes that are not exclusive to diabetes were type of filling, post-operative follow-up periods, level of necrosis, level of filling and perioperative conditions. However, more studies are needed to assess these factors as pooling of different diseases with the same factors will affect the significant results. Besides, studies that assessed factors affecting the extraction of root filled teeth in diabetic patients did not report these factors as significant ones.

Conclusion

Diabetes mellitus is considered one of the main risk factors for the failure of root canal therapy. However, its effect is minimal if it is combined with preoperative preparation and the state of necrotic teeth. All the results supported the fact that diabetes did not cause the failure of the root canal therapy, but it just delayed the healing process.

Recommendation for Future Work

Based on this review, more case-control studies are needed to understand factors affecting the influence of diabetes on the teeth healing and survival process for the root canal treatment. Most studies only assessed the influence of diabetes on the healing process; however, they did not investigate factors enhancing the healing and decreasing teeth extraction in these patients. More studies will provide a guideline for root canal treatment in diabetic patients.

Conflict of Interest

None.

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