

*Review Article*

**Evaluation of Association Between Infection of Endodontic Origin, Their Management and Systemic Health: A Narrative Literature Review**

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**Abstract:**

**Objective:** The most common dental condition is root canal infection. A focal infection is a localised or widespread infection that is caused by the systemic spread of microbes or their metabolites from one or more different foci of infection. A focus of infection, which is described as "a restricted area that is continuously infected with hazardous bacteria," may exist everywhere in the body. In the literature on medicine and dentistry, the tonsils, adenoids, oral tissues, and other structures have all been considered as potential infection sites. This review will evaluate the current research on the dynamic relationships between infections of endodontic origin, endodontic therapy, and overall health in light of new information that has since come to light. **Methods and materials:** A comprehensive search was conducted for all non-grey literature published using the online platforms PubMed, MEDLINE, and Scopus, web of sciences. To make sure that all pertinent studies were found, the succeeding search keywords were applied.: "endodontic infections", "systemic conditions", "management", "apical periodontitis", "diabetes", "hypertension". Furthermore, all appropriate scientific papers on role of endodontic infections and their management in different systemic diseases were included. 18 articles were included in the review. **Results:** Articles showed that the advancement and progression of CVDs have been linked to higher concentrations of inflammatory markers in individuals with periodontitis at root apex, according to a number of systematic reviews and meta-analyses. Persistent periodontitis at root apex may influence the onset and development of atherosclerosis through a number of different possible mechanisms. The literature provides significant support for the notion that people with DM had higher rates of apical periodontitis, larger periapical lesions, and more periapical infections than patients without diabetes. **Conclusion:** There is growing evidence that prolonged apical periodontitis-related bacteraemia and reduced inflammatory cytokines may have a deleterious impact on systemic health, including CVD development, autoimmune disorders, and diabetic metabolic dysregulation.

**Keywords:** Endodontic infections, systemic conditions, management, apical periodontiti

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**Introduction:**

The variety of the endodontic microbiology and its host relationships constitute not only a special challenge to therapy but also a possible danger for systemic disorders in other sections of the body. Endodontic

infections are polymicrobial infections. A dynamic aftereffect of infection of root canal is prolonged periodontitis at root apex. It is fueled by periapical tissue-specific persistent localised inflammation, which can cause accelerated bone loss and the development of periapical lesions.<sup>1-4</sup> If

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unchecked, this can develop into a sinus tract and result in cyst formation. With the assistance of different cell types and mediators of inflammation, the adaptive immune system and innate immune systems are activated in a condition known as apical periodontitis, which ultimately results in the loss of tissue at root apex and the development of periapical pathologies. The root canal system's microbiology, microbial pathogenic agents, and the human immune reaction interact in a complicated way to cause apical periodontitis.<sup>5-7</sup>

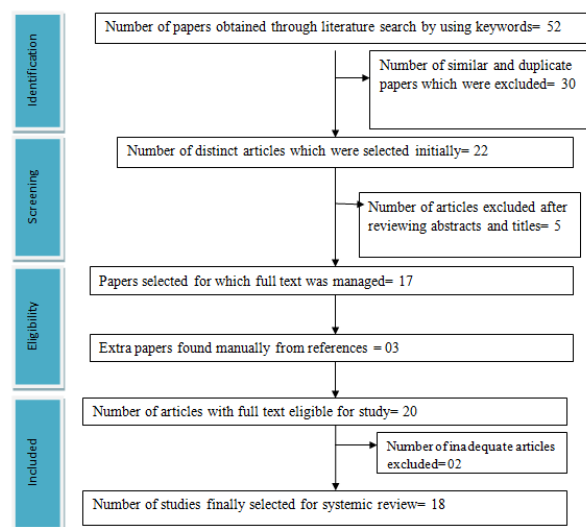
The burden of periodontitis at periapical region is significant worldwide. Nearly 23 million endodontic procedures are reportedly performed each year in Europe. Additionally, a systematic review revealed that apical periodontitis is highly prevalent worldwide ( 5 percent of of all tooth, one periapical infection per patient).<sup>8-12</sup> These figures show that root canal infection is one of the most prevalent dental disorders, which could put more strain on overall health and raise the expense of healthcare services globally. A localised or widespread infection known as a focal infection is one that is brought on by the systemic dissemination of microorganisms or their byproducts from some of the other centers of infection. Anywhere in the body, there might be a focus of infection, which is defined as "a limited area that is continuously contaminated with harmful microorganisms". The tonsils, adenoids, oral tissues, and other structures have all been mentioned as potential sites of infection in medical and dentistry literature.<sup>13-16</sup> The 'Focal Infection Era in Dentistry', when the focal infection theory reached its pinnacle of acceptance, spanned the late nineteenth century and early twentieth centuries. Rheumatoid arthritis and tooth health were closely interlinked at this time of focused infection.<sup>17-20</sup>

As a result, the extraction of teeth, removal of adenoids, removal of tonsils, and other organs was widely practised for many years in an effort to treat numerous inexplicable ailments that were thought to be brought on by localised infection. Numerous research have tried to figure out whether endodontic illness, a localised mouth infection, could affect the host immune response, endangering people's overall health. Although there have already been reviews on this topic, this review will evaluate the current research on the dynamic relationships between periodontitis at root apex, endodontic therapy, and overall health in light of new information that has since come to light.<sup>21</sup>

**Methods and Materials:**

A comprehensive search was conducted for all non-grey literature published using the online platforms PubMed, MEDLINE, and Scopus, web of sciences. To make sure that all pertinent studies were found, the succeeding search keywords were applied.: “endodontic infections”, “systemic conditions”, “management”, “apical periodontitis”, “diabetes”, “hypertension”. Furthermore, all appropriate scientific papers on role of endodontic infections and their management in different systemic diseases were included. There wasn't any specific time constraint for article to be included. We augmented our search by looking through the reference lists of every included publications for supplemental relevant studies. The review included different types of research, literature reviews, systematic review, systematic review and meta analysis.

The number of paper obtained through literature search by using keyword was 52. The number of distinct articles which were selected initially was 22. Then 5 articles were excluded after reviewing abstracts and titles. The number of papers selected for which full text was managed was 17. Extra papers that were found manually from cross checking of references. The number of articles with full text eligible for study was 20. However 02 articles were found inadequate on final screening. In the end 18 studies were included in this systematic review. (figure 1)



**Figure 1: Systematic representation of selection of articles in review**

**Results:**

The observations and inferences of the papers included in the literature review are presented below in table no 1.

**Table 1: Important details of articles included in the review**

<b>Authors details</b>	<b>Observations</b>	<b>Method used for study</b>
Byon et al. (2020) <sup>23</sup>	Periodontitis can raise the likelihood of coronary atherosclerosis and that preventing it may help lower that risk	Retrospective research
Baumgartner, J.C. et al (1976) <sup>29</sup>	3.3% cases following non-surgical root canal therapy, 33% cases following periapical curettage, 83.3% cases following surgical flap removal, and 100% cases following tooth extraction showed bacteremia.	Culture-based approach
Heimdahl, A et al (1990) <sup>55</sup>	20% cases after root canal therapy 100% cases following tooth extraction 70% cases following dental scaling showed bacteremia	Culture-based approach
Debelian, G.J. et al (1998) <sup>57</sup>	Anaerobic bacteria were present in all root canals. From 31 percent to 54 percent of the total patients had bacteremia.	Phenotypic and genotypic approach
Savarrio, L et al (2005) <sup>33</sup>	Thirty percent of patients involved bacteremia.	Culture-based approach
Reis, L.C et al (2016) <sup>34</sup>	After non-surgical therapy of infected root canal, bacteraemia was found in every patient that had been previously tested negative for it using a culture-based method.	Molecular approach (qPCR)
Tibúrcio-Machado CS et al 2021 <sup>58</sup>	In adults around the world, apical periodontitis affects at least one tooth. Although it is more common in samples from dental care providers, the frequency of apical periodontitis is equally significant in specimens from the overall population that are representative of the wider community. The study results should call attention to the concealed load of endodontic illness in the global population among health officials, the medical professionals, and dentistry professions.	Systematic review and meta analysis
Murray, C.A et al 2000 <sup>11</sup>	Scientists have been able to demonstrate that bacteria retrieved from the peripheral circulation after root canal therapy came mostly from root canal due to enhanced analytical techniques using advanced molecular biology approaches and improved culture methodologies.	Literature review

Wang, C.H et al 2011 <sup>20</sup>	Individually, diabetes mellitus condition, hypertension condition, and chronic artery disease condition are each significantly and positively related with a heightened incidence of tooth extraction following nonsurgical root canal therapy. Additionally, in addition to certain other confounding variables, the spectrum of systemic illness load also demonstrates the importance.	Prospective study
Segura-Egea, J.J et al 2010 <sup>19</sup>	When compared to matched participants lacking hypertension, the frequency of periodontitis at root apex and the need for endodontic therapy in patients with condition of hypertension was not substantially different.	Cross sectional research
Caplan, D.J et al 2006 <sup>22</sup>	Results of this study point to links connecting prolonged periodontal inflammation and CHD onset, particularly in younger males.	Longitudinal research
Pasqualini D et al 2012 <sup>59</sup>	In comparison to healthy counterparts, CHD participants showed a greater frequency of oral illnesses and lesser adherence to oral preventative measures. A non-traditional vulnerability for CHD, chronic dental disorders may increase the likelihood of CHD.	Case control study
Liljestrand, J.M et al 2016 <sup>24</sup>	Endodontic lesions have a separate relationship with CAD, and more specifically, acute coronary syndrome. Given the high frequency of endodontic lesions and CAD, this is highly relevant from the standpoint of public health.	Cross sectional research
Jiménez-Sánchez MC et al 2020 <sup>12</sup>	The findings are contradictory, making it impossible to establish a link between CVDS and endodontic illness. The risk variables shared by both diseases can complicate the analysis and skew the findings. To establish the temporal relationship and the dose-response gradient, longitudinal epidemiological studies must be conducted in order to draw firm conclusions about the type of association (causal or non-causal) between the two diseases.	Narrative review
Oe Y et al 2009 <sup>15</sup>	Statin treatment, glycemic sensitivity, and periodontal different metrics were identified as separate, significant predictors for CAD by multivariate analysis. Aggregate periodontal hazard ratings were substantial, independent predictors of CAD.	Cross sectional research
Costa TH et al 2013 <sup>47</sup>	Chronic periodontitis at root apex was independently correlated with coronary artery disease in these research participants..	Cross sectional research

Garg P et al 2016 <sup>9</sup>	Our findings point to an independent relationship between periodontitis at root apex and cardiovascular illnesses. Since the investigations used population that was challenging to compare and had weak risk criteria, it was unable to demonstrate a causal association. Additional confounding factors were also not ruled out.	Narrative review
Berlin-Broner Y et al 2016 <sup>10</sup>	Although the majority of published research discovered a link among periodontitis at root apex and heart disorders, the reliability of the available information is medium to low, making it impossible to determine a cause-and-effect connection.	Systemic review

**Discussion:**

CVDs are one of the main cause of death globally, accounting for nearly 30% of all deaths worldwide, CVDs place a strain on global health and the economy. Additionally, it is anticipated that over the next twenty years, the occurrence of CVDs would rise by around 10%, tripling the expense of healthcare.<sup>22-25</sup>

Endodontic infections and coronary heart disorders, the most prevalent form of CVDs accounting for 49 percent of the occurrence of CVD, have been linked in studies. For instance, An G.K. et al revealed that individuals with periodontitis at root apex are 5.3 times more susceptible to CVDs than individuals without periodontitis at root apex in a hospital records-based analysis.<sup>35</sup> Additionally, the connection was clear in the study conducted via Virtanen et al.<sup>36</sup> However, both research included individuals who smoked, which is another CVD risk factor. The relationship between periodontitis at root apex and CVDs has received a lot of attention over the past ten years.<sup>26-34</sup> The likelihood of cardiovascular catastrophes may increase because higher inflammatory biomarker concentrations can cause a systemic response of inflammation.<sup>37</sup>

The advancement and progression of CVDs have been linked to higher concentrations of inflammatory markers in individuals with periodontitis at root apex, according to a number of systematic reviews and meta-analyses. The connection between periodontitis at root apex and CVDs is weak, according to recent research by Jakovljevic et al in an overarching review, and the authors emphasised the need for further, carefully

planned, longitudinal controlled research to enhance the evidence and support a possible association.<sup>38</sup>

Persistent periodontitis at root apex may influence the onset and development of atherosclerosis through a number of different possible mechanisms. First off, endodontic microorganisms may be directly sown into the artery wall through bacteremia, causing a local inflammatory reaction and adaptive immune reaction as well as cellular modifications that eventually lead to the formation of atherosclerotic lesions. Secondly, endothelial malfunctioning and the development of the atherosclerotic inflammation reaction may result from dampening of endodontic microbiological end products or localized inflammatory cytokines in the circulatory system. In atherothrombotic patches or vascular biopsies, several investigations have found both oral bacteria and indicators. Consequently, the establishment of CVDs may be affected by the existence of septicemia and the limited systemic inflammation linked to persistent periodontitis at root apex.<sup>39,40</sup>

Diabetes mellitus (DM) can affect a person's immune system, predisposing them to condition of chronic inflammation, gradual tissue degeneration, and undermined tissue regeneration capacity. Diabetes can eventually cause a number of organs, including, nerves, kidneys, blood vessels, eyes, and the heart, to become dysfunctional.<sup>41-45</sup>

Additionally, the findings revealed higher pulpal inflammation and decreased dentin bridge development. The literature provides significant support for the notion that people with DM had higher rates of apical periodontitis, larger periapical lesions, and more periapical infections than patients

without diabetes. Patients with DM had a higher likelihood of unresolved periapical lesions and ineffective endodontic treatment, according to a retrospective study by Segura-Egea et al.<sup>45</sup> In addition to flare-ups in all diabetic patients, there was a pattern toward more symptomatic periradicular illness in insulin-treated diabetic individuals.<sup>46-48</sup>

On the contrary, other research findings imply that chronic periapical illness promotes to diabetic metabolic unregulation and is associated with elevated HbA1C concentration. Diabetes patients have an elevated inflammatory response at periapical area, which raises blood sugar levels and worsens diabetes, necessitating an increment in insulin dosing or treatment modification. Yip et al. (2021) presented evidence connecting diabetes mellitus (DM) and the degree of glycemia to the rise in apical periodontitis prevalence. Due to their associations with lower prevalences of apical periodontitis, the study also suggested that statin utilization and metformin utilization may be preventative in this connection.<sup>46</sup>

Aside from that, the existing scientific research strongly implies that DM has a detrimental effect on the success of endodontic therapy in regards of periapical healing because it causes the repair of the periapical tissue to be delayed or stopped. According to Ng et al. (2011), root-filled teeth have DM as one of their predictive markers for survival.<sup>47</sup> In cases where patients with DM have preoperative periradicular abnormalities, the effectiveness of endodontic therapy is reduced. Diabetics have a worse prognosis for root-filled teeth, with a greater frequency of root canal therapy failure and a higher frequency of chronic periodontitis at root apex that persists. As a result, diabetes lowers the preservation of teeth with roots filled in and increases the likelihood of tooth extraction following non-surgical therapy of infected root canal.

Dental professionals should be conscious of the possible link involving diabetes and infections of endodontic origin as diabetes is considered as the third most widespread chronic medical disease among patients who require dental care. Informed consent should cover this, and care planning should incorporate communication with the patient's doctor.<sup>48-49</sup>

Periodontitis at root apex is more common in autoimmune diseases like IBD and RA, according to studies. Similar results were recently reported by Ideo et al, who found that individuals with autoimmune illnesses (RA, Ps, and IBD) had an increased concentration of apical periodontitis than the controls.<sup>50-51</sup> This may be explained by how both disorders arise, advance, and persist despite the overproduction of common inflammatory markers such TNF- inflammatory biomarker, IL-1 inflammatory biomarker, IL-6 inflammatory biomarker, IL-23 inflammatory biomarker, and IL-17 inflammatory biomarker.<sup>52</sup>

In individuals with autoimmune illnesses taking bDMARDs, Piras et al research revealed a considerably greater occurrence of molars with periodontitis at root apex.<sup>52</sup> Similar findings were found in a recent study by Ideo et al, which found that biologic medication-using patients with autoimmune illnesses had a higher likelihood of periodontitis at root apex.<sup>51</sup> Faster healing following endodontic treatment for molars with periodontitis at root apex in subjects receiving biologic drugs than in controls was demonstrated by Cotti et al., indicating that immune-modifying therapy may affect how quickly the condition heals after treatment.<sup>53</sup> Therefore, the occurrence of periodontitis at root apex and the prognosis following endodontic treatment may be affected in patients with autoimmune disorders as a result of altered immune responses and the action of immune modulatory treatments.<sup>54-59</sup>

Some researchers have attempted to link apical periodontitis with a variety of systemic problems, such as liver disorders and haemophilia, albeit this has not yet been proven. When contrasted to healthy controls, 79 percent of the survey respondents had one or more than one apical periodontitis, according to a cross-sectional research by Castellanos-Cosano et al. that looked at the prevalence of periodontitis at root apex among participants undergoing liver transplant evaluation. Additionally, the same group of writers looked into how common apical periodontitis was in people with genetic haemophilia and discovered that nearly 68 percent of those people had the disease.<sup>54</sup>

The results of these studies strongly suggest that periodontitis at root apex occurs in a number of systemic diseases, necessitating frequent dental checkups and encouragement of oral hygiene practises in medically fragile patients in order to not only improve and maintain these patients' oral health but also lessen the systemic load of dental disorders in these caregivers.

### Conclusions:

There is growing evidence that prolonged apical periodontitis-related bacteraemia and reduced inflammatory cytokines may have a deleterious impact on systemic health, including CVD development, unfavourable pregnancy complications, and diabetic metabolic dysregulation. Although the evidence is weak, it suggests that patients with illnesses like diabetes mellitus or autoimmune disorders affect not just the prognosis following endodontic therapy but also the occurrence of apical periodontitis. By encouraging apical periodontitis repair, statins may be preventative in this connection.

Furthermore, strong evidence dispels the myths originating from research conducted 70–80 years old about the connection between endodontic therapy and focal inflammation, which led to evidence in support of tooth extraction, and demonstrates that effective root canal therapy improves systemic well-being by the inflammatory burden. To strengthen the existing data supporting the advantages of endodontic therapy on systemic health, more high-quality research is necessary.

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