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Comparative Analysis of The Relationship between Periodontitis and Cardiovascular Diseases: A Review

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Abstract

Periodontitis and cardiovascular diseases are prevalent conditions in today's society. The review underscores both the similarities and disparities in prevalence rates, risk factors, and underlying mechanisms, offering insight into the intricate interplay between these two conditions. This study also aims to investigate the possible associations between periodontitis and cardiovascular diseases. Research has demonstrated that, even in the absence of known cardiovascular risk factors, periodontal disease is linked to CRP. In response to inflammatory cytokines, the liver is the primary site of production for 12- 14 CRP, an acute-phase reactant. Cross-sectional evidence from over a dozen prospective epidemiologic studies showed that CRP was predictive of subsequent vascular events, such as stroke, myocardial infarction, peripheral artery disease, and sudden cardiac death. The relationship between periodontal disease and levels of CRP and IL-6 in racial/ethnic minority groups—especially in the different population—has not received much attention in the literature, despite the abundance of research on the relationship between periodontal disease status and CVD biomarkers." It may be possible to assess periodontal tissue degeneration and forecast the risk of cardiovascular disease in these patients by using several clinical indicators such as CRP level and IL-6.

Keywords: Periodontitis, Cardiovascular Diseases, Inflammation, Dietary Pattern, Infection, C-Reactive Protein (CRP).

Introduction

An overview of (CVDs) and Periodontitis: Cardiovascular diseases (CVDs) are a major global cause of death, accounting for 17.9 million deaths annually (or 31% of all deaths [1,2]. Cardiovascular diseases are leading cause of death in India and United states of America. Based on an analysis of data from the National Health

and Nutrition Examination Survey (NHANES) spanning from 2009 to 2014, it's estimated that approximately 42% of dentate adults aged 30 years or older in the United States exhibit some degree of periodontitis (mild, moderate, or severe). Similarly, a multicentric oral health survey conducted under the Government of India and the World Health Organization collaborative program in 2004 aimed to establish baseline data, revealing that around 51% of individuals have some form of periodontitis.[3,4] Exploring the potential link between periodontitis and cardiovascular disease (CVD) is crucial, considering their shared inflammatory pathways and risk factors. Numerous investigations have documented a favorable correlation between periodontitis and cardiovascular disease (CVD) in populations of Indian and American descent. According to an Indian study, people with severe periodontitis were more likely than people without or with mild periodontitis to develop coronary artery disease (CAD). In a similar vein, research conducted in the United States has discovered that periodontitis significantly predicts cardiovascular disease (CVD), which includes peripheral artery disease, heart attack, and stroke.[5–7]

Methodology

Objective of the Review

The primary objective of this review is to analyze and summarize existing research on the association between periodontitis and cardiovascular diseases, focusing on potential mechanisms, common inflammatory pathways, and biomarkers like C-reactive protein (CRP). The review aims to compare findings from diverse populations (e.g., Indian, American, European), providing a global perspective on the correlation.

Search Strategy

- Databases: The literature search will include multiple databases such as:
- PubMed
- MEDLINE
- Scopus
- Cochrane Library
- Google Scholar
- Boolean Operators: Boolean operators (AND, OR) will be used to refine the search strategy. Example: ("Periodontitis" AND "Cardiovascular diseases") OR ("Inflammation" AND "CRP" AND "Atherosclerosis").
- Time Frame: The search will be restricted to articles published between 2000 and the present to capture the most recent data on the subject. However, older seminal works may be included if they are foundational to understanding the link between periodontitis and CVD.

Data Extraction

A standardized data extraction form will be used to gather information from the selected studies. Data to be extracted include:

- Study details: Author, year, country, study design, sample size.
- Population characteristics: Age, gender, health status, and geographic location.
- Periodontitis-related variables: Severity of periodontitis, diagnostic criteria, periodontal pathogens.
- CVD-related variables: Types of cardiovascular diseases (e.g., coronary artery disease, stroke), diagnostic criteria, clinical outcomes.
- Biomarkers: CRP levels, IL-6, and other relevant inflammatory markers.
- Key findings: Association between periodontitis and CVD, statistical significance, and reported mechanisms.

Data Synthesis

- Qualitative Analysis: The extracted data will be synthesized qualitatively, focusing on recurring themes and patterns across studies. Special attention will be given to the inflammatory mechanisms linking periodontitis and CVD, the role of CRP as a biomarker, and variations across populations.
- Comparative Analysis: The review will compare studies from different regions (India, U.S., Europe) to highlight geographical differences in the prevalence and severity of periodontitis and CVD, as well as how these affect the correlation.
- Mechanistic Discussion: The review will analyze biological pathways, focusing on inflammation, endothelial dysfunction, and bacterial translocation as mediators of the relationship between periodontitis and CVD.

Risk of Bias Assessment

Although this is a narrative review, the quality of the included studies will be assessed. The Newcastle-Ottawa Scale (NOS) will be used to evaluate the quality of observational studies, and the Cochrane Risk of Bias tool will be employed for RCTs. Studies with a high risk of bias will be included in the review but flagged and considered in the interpretation of the results.

Result

This review's findings demonstrates the strong correlation between periodontitis and cardiovascular diseases (CVD), with inflammation serving as a key mediator between the two illnesses. The severity of periodontitis and the elevated risk of cardiovascular events, such as coronary artery disease, stroke, and atherosclerosis, are consistently correlated with elevated levels of inflammatory biomarkers, such as C-reactive protein (CRP) and interleukin-6 (IL-6). Smoking, poor dental hygiene, and systemic inflammation are examples of shared risk factors that highlight the relationship even more.

Studies across various populations reveal that patients with advanced periodontitis often exhibit higher CRP levels, even after controlling for traditional CVD risk factors such as smoking, hypertension, and diabetes. Clinical trials have also shown improvements in endothelial function and reductions in CRP following periodontal therapy, further supporting the causal link.

Moreover, the review highlights how bacterial translocation, systemic inflammation, and immune dysregulation contribute to the pathophysiology of cardiovascular diseases in individuals with chronic periodontitis. The variability in findings between different ethnic groups and regions suggests that genetic, environmental, and lifestyle factors also play a role, underscoring the importance of population-specific studies and interventions.

Discussion

Periodontitis and CVD

ADA defines Periodontitis as “Periodontal disease is a chronic infection that can result in the destruction of tooth-supporting structures (i.e., the gingiva, periodontal ligament, and/or alveolar bone) and eventual tooth loss. It is a multifactorial infectious disease influenced by several risk factors such as genetics, environment and the host immune system.[8] Although microorganisms are implicated as the etiologic agent responsible for the inflammatory lesion, the products of inflammation play an important role in the loss of connective tissue as well as in the loss of supportive alveolar bone.

CVDs definition & characteristics

The American Heart Association defines cardiovascular diseases (CVD) as a group of conditions that affect the heart and blood vessels, including coronary artery disease, heart failure, stroke, and high blood pressure.

These conditions can lead to serious complications and have a significant impact on overall health and quality of life. Preventive measures such as adopting a healthy lifestyle, managing risk factors like high cholesterol and hypertension, and seeking prompt medical attention are crucial in reducing the burden of cardiovascular diseases.[9]

The liver produces C-reactive protein (CRP), an acute-phase protein, in reaction to inflammation. It has a complex and important association to cardiovascular disease (CVD):

Marker of Inflammation: An important mechanism in the initiation and advancement of atherosclerosis, the main cause of CVD, is inflammation, which is indicated by elevated CRP levels. Plaque accumulation in the arteries due to persistent inflammation raises the risk of heart attacks and strokes.[10]

Predictive Value: Even in those who don't exhibit any outward signs of cardiovascular disease, elevated CRP levels are linked to a higher chance of subsequent cardiovascular events. Lower levels of the protein can be found via high-sensitivity CRP (hs-CRP) testing, which improves the risk assessment for CVD.[11]

Therapeutic Target: Although CRP is mainly a marker, there is evidence that it is directly involved in the pathophysiology of cardiovascular disease. Further research is required to establish the potential reduction of cardiovascular risk by anti-inflammatory medications that lower CRP levels.[12]

Overall, CRP is a significant biomarker for cardiovascular health that helps with the diagnosis, treatment, and prognosis of cardiovascular illness.

Mechanism and association between CVDs and Periodontitis

The following could be potential mechanisms: endothelial dysfunction, bacterial translocation, and inflammation as they relate to periodontitis and CVD. One of the risk factors for CVD is atherosclerosis, which can arise as a result of periodontitis-induced inflammation. Improved blood flow can raise the risk of cardiovascular disease (CVD) due to endothelial dysfunction brought on by periodontitis. The spread of bacterial toxins into the circulation as a consequence of periodontitis-induced bacterial translocation might induce systemic inflammation and raise the risk of cardiovascular disease (CVD).

Chronic gum inflammation, or periodontitis, has been connected in a number of ways to cardiovascular disease (CVD), including through its association with C-reactive protein (CRP). [1,7]This is how they are related to one other:

Systemic Inflammation: Inflammatory indicators such as CRP are raised as a result of the systemic inflammatory response that is sparked by periodontitis. One well-established risk factor for the onset and advancement of atherosclerosis—the accumulation of plaque in the arteries that causes CVD—is chronic inflammation.

Increased CRP Levels: As a reaction to inflammation, periodontitis can raise CRP levels. Elevations in CRP are linked to a higher chance of cardiovascular disease (CVD), which makes CRP a valuable biomarker for determining cardiovascular risk in those with periodontal disease.[13,14]

Atherosclerosis and Plaque Formation: Atherosclerosis can be initiated and progressed in part by the inflammation brought on by periodontitis. One of the main mechanisms in CVD is the promotion of inflammation and plaque formation in the arteries by bacteria from periodontal diseases that can reach the bloodstream.

Endothelial Dysfunction: Endothelial dysfunction is a disorder in which the inner lining of blood vessels

malfunctions. It is often brought on by chronic inflammation from periodontitis. Atherosclerosis and other cardiovascular diseases start with this dysfunction.

Several studies have demonstrated that people with periodontitis have elevated CRP levels and are more vulnerable to cardiovascular events including strokes and heart attacks. Reductions in CRP levels and enhancements in endothelial function have been linked to periodontitis treatment, indicating a possible benefit for cardiovascular health.[6]

The comparative study of the populations around the world is especially significant because of the variations in the incidence and severity of CVDs and periodontitis in these two groups. Numerous studies have explored the link between periodontal disease and cardiovascular disease, consistently finding positive associations even after adjusting for multiple risk factors. Understanding this connection across diverse demographics can significantly improve intervention and treatment strategies.[5]

Table 1:

Author, Year of study	country	Study design	Age of experimental group	Population	Biomarkers assessed	Conclusion
A Sharma, M Astekar, 2014 sharma(15)	India	RCT	25-60	Indian	CRP	significantly higher levels of CRP .CRP levels among periodontitis patients
Nicole Delange1 Suzanne Lindsay, 2017(16)	USA	Cross-sectional	21-43	American Indian/ Alaskian	CRP, IL-6	This study shows that in this relatively young adult AI/AN population, increasing levels of IL-6 are linked to moderate periodontal disease. But could not provide a significant relationship between CRP and periodontitis
A. Pejcic, L. J. Kesic & J. Milasin, 2011 (17)	Serbia	RCT	23-58	Serbian	CRP	This study was able to indicate that elevated CRP levels tended to be more closely related to gingival bleeding, poor oral hygiene and the presence of periodontal microorganisms (P. gingivalis and A. actinomycetemcomitans)
D'Aiuto F,	UK	Cross-sectiona	37-55	UK	CRP,IL-6	This study indicated Serum

Ready D, Tonetti MS,2004(18)						concentrations of the tested inflammatory markers, IL-6 and CRP, were significantly correlated with the extent and severity of periodontitis
Salde, Elissa .M Ghezzi,2003(19)	USA	Cross-sectional	52-75	USA	CRP	The results of this study demonstrated elevated concentration of serum CRP in individuals with extended periodontitis

Further Mechanistic Insights and Emerging Evidence: Recent studies continue to strengthen the understanding of biological mechanisms connecting periodontitis and cardiovascular diseases (CVDs). Beyond CRP and IL-6, other biomarkers such as tumor necrosis factor-alpha (TNF-α), matrix metalloproteinases (MMPs), and fibrinogen have been identified as key players in systemic inflammation initiated by periodontitis. These molecules can significantly influence vascular integrity and accelerate the atherosclerotic process.[20,21]

Immune Dysregulation and Vascular Impact: Periodontitis triggers a dysregulated immune response, characterized by excessive neutrophil activity and upregulated pro-inflammatory cytokines. These immune responses contribute to vascular endothelial activation and damage. When the endothelial lining becomes dysfunctional, it fails to regulate vascular tone and permeability effectively, thereby facilitating lipid infiltration and plaque formation within arterial walls.

Bacteremia and Direct Pathogen Involvement: Transient bacteremia, commonly observed during activities like tooth brushing or dental procedures in patients with periodontitis, allows periodontal pathogens like Porphyromonas gingivalis and Aggregatibacter actinomycetemcomitans to enter systemic circulation. These microorganisms can localize within atherosclerotic plaques, as demonstrated by PCR and immunohistochemical studies, suggesting a direct microbial contribution to plaque development and instability.[22]

Molecular Mimicry and Autoimmunity: Emerging research highlights the role of molecular mimicry in the development of autoimmune responses in CVD. Antigens from periodontal bacteria may resemble host antigens, leading to the production of autoantibodies that damage vascular tissues. This autoimmune mechanism may partly explain the persistent inflammation and progression of atherosclerosis in patients with periodontal disease.[23]

Public Health Significance and Socioeconomic Considerations

Periodontitis and CVDs share not only biological mechanisms but also social determinants of health, including socioeconomic status, education, access to healthcare, and lifestyle behaviors. This intersection significantly affects global disease burden, especially in low- and middle-income countries.

Health Inequities: Populations in rural and underserved areas often face barriers to both dental and cardiovascular care, resulting in delayed diagnosis and management. These disparities compound the risk of developing chronic conditions and experiencing adverse outcomes.

Economic Burden: The co-occurrence of periodontitis and CVD leads to increased healthcare utilization and expenditure. Managing advanced stages of both conditions requires costly interventions, including cardiac surgeries and periodontal surgeries, underscoring the importance of early preventive care and integrated management.[24]

Educational Campaigns: Public awareness initiatives promoting oral hygiene and heart health can play a vital role in primary prevention. Programs aimed at educating patients about the systemic implications of oral health, particularly in high-risk communities, may help reduce the incidence of both conditions.

Clinical Implications and Multidisciplinary Management

The bidirectional relationship between oral and cardiovascular health necessitates a collaborative approach between medical and dental professionals. Early screening, shared electronic health records, and coordinated care models are essential in addressing this interconnection.

Role of Dental Professionals: Dentists and periodontists should consider systemic risk assessment as part of periodontal evaluation. Incorporating CRP or other inflammatory marker testing in dental clinics could provide valuable insights into a patient's cardiovascular risk profile.

Role of Cardiologists and Primary Care Providers: Cardiologists and primary care physicians should be aware of periodontal health as a potential modifiable risk factor for CVD. Referrals to dental professionals for patients with uncontrolled cardiovascular risk factors could form part of routine care.

Evidence from Interventional Studies: A number of clinical trials suggest that periodontal treatment, including scaling and root planing (SRP), significantly reduces systemic inflammation. For instance, Tonetti et al. (2007) demonstrated a reduction in CRP and improved endothelial function following intensive periodontal therapy in otherwise healthy patients.[18]

Future Research Directions: Despite strong associative evidence, questions regarding causality and intervention efficacy remain. Longitudinal, multi-center, randomized controlled trials with robust methodology are needed to explore:

Long-Term Impact of Periodontal Therapy: Future studies should assess whether sustained periodontal health translates into a decreased incidence of major adverse cardiovascular events (MACE) such as myocardial infarction and stroke.[25]

Personalized Risk Profiling: Research should explore genetic, microbiomic, and immunologic factors that may predispose certain individuals to both periodontitis and CVD. Understanding these individualized risk profiles could guide personalized prevention strategies.[26]

Novel Biomarkers and Diagnostic Tools: Advancements in salivary diagnostics and point-of-care testing offer non-invasive tools for early detection of systemic inflammation. Salivary CRP and IL-6 measurement could become part of routine screening for at-risk populations.[27]

Digital Health and AI Integration: The integration of artificial intelligence in analyzing large datasets from electronic health records can aid in identifying patterns and predictive factors linking oral and cardiovascular health. AI models could stratify patients based on periodontal and cardiovascular risk for proactive interventions.[28]

Conclusion

Treating periodontitis has the potential not solely to improve oral wellness but also to reduce systemic

inflammation and perhaps minimize the risk of cardiovascular challenges. In order to further understand the link between cause and effect and investigate the efficacy of anti-inflammatory treatments that target CRP and other indicators in lowering the risk of CVD in patients with periodontitis, future research should concentrate on longitudinal studies. Adopting action to address this relationship may have substantial effects on public health, particularly for populations where both illnesses are highly prevalent.

Given the shared pathophysiological pathways and modifiable nature of periodontitis, a multidisciplinary approach integrating dental and cardiovascular care is warranted. Dental professionals should be involved in chronic disease prevention strategies, while cardiologists should be aware of oral health as a contributing factor in systemic inflammation and vascular dysfunction.

Future research should concentrate on well-designed longitudinal studies. Additionally, public health initiatives promoting oral-systemic health education could have substantial impacts, especially in regions where both diseases are highly prevalent.

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