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PERIODONTITIS AND OSTEOPOROSIS-A BIDIRECTIONAL RELATIONSHIP IN BONE RESORPTION: AN OVERVIEW

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Abstract
Periodontitis and osteoporosis are two distinct but interconnected conditions characterized by bone resorption and structural deterioration. Periodontitis is a localized chronic inflammatory disease affecting the supporting tissues of the teeth, while osteoporosis is a systemic skeletal disorder marked by reduced bone mass and fragility. Recent clinical and epidemiological evidence suggests a strong bidirectional relationship between these conditions, particularly in populations with shared risk factors such as postmenopausal women and the elderly. Both conditions share common pathophysiological pathways, notably the RANK/RANKL/OPG signaling axis and inflammatory cytokines such as IL-1, IL-6, and TNF-α. These mediators contribute to increased osteoclast activity, impaired osteoblast function, and accelerated bone turnover. Additionally, nutritional deficiencies, hormonal imbalances, smoking, alcohol use, and systemic diseases such as diabetes further exacerbate the progression of both diseases. Diagnostic modalities such as bone mineral density testing, periodontal indices, and emerging salivary and serum biomarkers facilitate early detection and monitoring. Therapeutic strategies include anti-resorptive medications, calcium and vitamin D supplementation, scaling and root planning, and antimicrobial treatments. An interdisciplinary management approach is essential for optimal patient outcomes. This review provides a comprehensive overview of the molecular, clinical, and diagnostic evidence linking periodontitis and osteoporosis. It emphasizes the importance of integrated healthcare delivery, future research into shared biomarkers, and the potential for personalized medicine in managing at-risk populations. Understanding this complex interplay will not only improve disease outcomes but also contribute to preventive public health strategies targeting bone and oral health.

Keywords: Periodontitis; Osteoporosis; RANK/RANKL/OPG; Inflammation; Bone resorption; Cytokines; Diagnostic biomarkers; Multidisciplinary management.

Introduction
Periodontitis is a chronic inflammatory disease that affects the supporting structures of the teeth, including the gingiva, periodontal ligament, cementum, and alveolar bone. It is primarily initiated by bacterial biofilms (dental plaque) that trigger an immune-inflammatory response, leading to the progressive destruction of periodontal tissues and ultimately tooth loss if left untreated. Osteoporosis, on the other hand, is a systemic skeletal disorder characterized by low bone mass, deterioration of bone tissue, and increased bone fragility, making bones more susceptible to fractures. While periodontitis is considered a localized condition affecting the oral cavity, osteoporosis is a systemic condition that affects the entire skeletal framework. However, both conditions share a common hallmark-bone resorption-and may influence each other through underlying inflammatory and hormonal pathways [1, 2].

The global burden of both diseases is substantial and increasing, particularly in aging populations. Periodontitis affects more than 50% of adults worldwide, while osteoporosis is estimated to affect over 200 million people, particularly postmenopausal women. Both conditions contribute to a decline in quality of life, increased healthcare costs, and complex treatment challenges [3]. The prevalence of both diseases in the same individual, especially in postmenopausal women and the elderly, has prompted researchers to explore a potential connection between the two. Several epidemiological, clinical, and experimental studies suggest a bidirectional relationship, wherein osteoporosis may exacerbate alveolar bone loss seen in periodontitis, and

chronic periodontitis may influence systemic bone turnover, potentially contributing to osteoporosis progression [4,5].

The rationale behind exploring this bidirectional link lies in their shared pathophysiological mechanisms, including the role of inflammatory cytokines, bone resorption mediators, and hormonal influences such as estrogen deficiency. Understanding these shared pathways can help in the early identification of individuals at risk, improve preventive strategies, and offer integrated therapeutic approaches that address both periodontal and skeletal health [6,7].

This review aims to provide a comprehensive overview of the relationship between periodontitis and osteoporosis, exploring their overlapping risk factors, molecular mechanisms, clinical evidence, diagnostic strategies, and current as well as emerging therapeutic options. By highlighting this interplay, the review emphasizes the need for interdisciplinary collaboration between dental and medical professionals to ensure holistic management of affected individuals and improve patient outcomes.

Pathophysiology of Periodontitis

Periodontitis begins with the accumulation of microbial plaque biofilms on the tooth surfaces, especially in the subgingival region. These biofilms consist primarily of Gram-negative anaerobic bacteria such as *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola*, which are known to produce virulence factors like lipopolysaccharides (LPS), proteases, and other toxins. These microbial products trigger an immune response from the host aimed at eliminating the pathogens. However, in susceptible individuals, this host response becomes dysregulated and exaggerated, resulting in collateral tissue damage rather than resolution of the infection [8].

A key aspect of the pathogenesis involves the activation of cytokine-mediated inflammatory pathways. Pro-inflammatory mediators such as interleukin-1β (IL-1β), tumor necrosis factor-alpha (TNF-α), and prostaglandin E2 (PGE2) are released in abundance, promoting recruitment of neutrophils, macrophages, and lymphocytes to the affected periodontal tissues. This sustained inflammatory environment enhances osteoclastogenesis via the RANK/RANKL pathway, tipping the balance toward bone resorption. In the process, not only is the alveolar bone degraded, but there is also progressive destruction of the periodontal ligament and connective tissue attachment to the tooth root, ultimately leading to tooth mobility and loss.

The destruction in periodontitis is therefore not merely a consequence of bacterial infection but results from a complex interaction between microbial challenge and the host's immune-inflammatory response. The persistent activation of matrix metalloproteinases (MMPs) further accelerates extracellular matrix degradation, contributing to the chronic and irreversible nature of the disease [9-12].

Pathophysiology of Osteoporosis

Osteoporosis is characterized by a systemic reduction in bone mass and deterioration of bone microarchitecture, which increases the risk of fractures. The fundamental pathological mechanism involves an imbalance in the bone remodeling cycle, where the activity of bone-resorbing cells (osteoclasts) surpasses that of bone-forming cells (osteoblasts). This imbalance leads to net bone loss over time, particularly in trabecular (spongy) bone, which is more metabolically active and thus more vulnerable to resorptive changes [13].

Estrogen deficiency plays a pivotal role in the pathogenesis of osteoporosis, especially in postmenopausal women. Estrogen has a protective effect on bone by inhibiting osteoclast formation and activity and by promoting osteoblast survival. When estrogen levels decline, the inhibition of osteoclastogenesis is removed, leading to increased bone resorption. Additionally, estrogen deficiency upregulates the production of pro-resorptive cytokines such as IL-1, IL-6, and TNF-α, which further activate the RANKL pathway, exacerbating osteoclast-mediated bone degradation [14].

Nutritional deficiencies, particularly of calcium and vitamin D, also contribute significantly to osteoporosis. Calcium is a critical component of bone mineral, and its deficiency leads to compensatory bone resorption to maintain serum calcium levels. Vitamin D is essential for calcium absorption and bone mineralization; its insufficiency not only impairs calcium metabolism but also contributes to secondary hyperparathyroidism, which accelerates bone turnover and loss. Thus, osteoporosis arises from complex interactions among hormonal, nutritional, and cellular factors, all converging to create a state of increased bone fragility and susceptibility to fractures, especially in the hip, spine, and wrist [15].

Common Risk Factors

Several risk factors are shared between periodontitis and osteoporosis, suggesting overlapping pathogenic mechanisms. Age is a predominant factor, as both diseases are more prevalent in the elderly due to degenerative changes in bone and immune response. Gender, particularly postmenopausal women, is critical due to the decline in estrogen levels, which significantly contributes to bone resorption and may exacerbate periodontal breakdown.

Hormonal changes, such as estrogen deficiency, not only impair bone density but also modulate the immune-inflammatory response, creating a favorable environment for periodontal tissue destruction. Nutritional deficiencies, especially calcium and vitamin D, hinder bone remodeling and mineralization, which are essential for maintaining both skeletal and alveolar bone health. Lifestyle factors like smoking and alcohol consumption further

compromise bone quality and immune function. Additionally, systemic diseases such as diabetes mellitus can amplify inflammatory responses and alter bone metabolism, aggravating both periodontitis and osteoporosis [16-18].

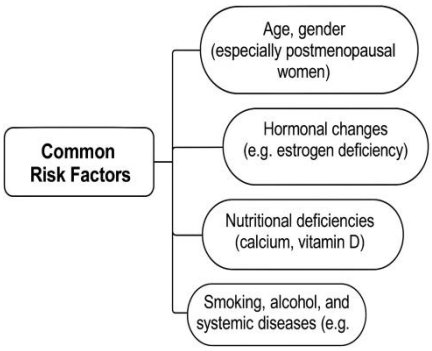

Fig.1: Flow for Common Risk Factors

Evidence for the Bidirectional Relationship

A growing body of clinical and epidemiological studies supports a bidirectional association between periodontitis and osteoporosis. Research shows that osteoporotic individuals are more prone to alveolar bone loss, which compromises tooth support and increases the risk of periodontitis. Conversely, chronic periodontitis may influence systemic bone metabolism through the release of inflammatory cytokines like IL-6 and TNF-α, which can promote osteoclastic activity beyond the oral cavity.

Studies have shown that osteoporosis can accelerate the progression of periodontal disease, especially in postmenopausal women, by reducing bone density in the jaw. Longitudinal and cross-sectional studies further validate this link, indicating that individuals with low bone mineral density (BMD) tend to exhibit worse periodontal outcomes. Meta-analyses and large population-based cohorts have consistently demonstrated that maintaining skeletal bone health is beneficial for periodontal integrity, and vice versa.

This interplay highlights the importance of a holistic approach in managing patients, especially those at risk for or already affected by either condition [19, 20].

Molecular and Cellular Mechanisms

The pathogenesis of both periodontitis and osteoporosis converges at a molecular level, particularly in the dysregulation of bone remodeling pathways. One of the most critical regulators is the RANK/RANKL/OPG signaling axis. Receptor Activator of Nuclear Factor Kappa-B Ligand (RANKL) is expressed by osteoblasts and activated T-cells and binds to its receptor RANK on osteoclast precursors, promoting osteoclastogenesis. Osteoprotegerin (OPG), a decoy receptor for RANKL, inhibits this interaction, thereby suppressing bone resorption. In both diseases, an imbalance favoring RANKL over OPG is observed, leading to enhanced osteoclastic activity and bone loss.

Additionally, pro-inflammatory cytokines such as interleukin-1 (IL-1), IL-6, and tumor necrosis factor-alpha (TNF-α) play pivotal roles. These cytokines not only amplify local inflammation in periodontal tissues but also stimulate RANKL expression, perpetuating bone resorption. Moreover, these inflammatory mediators are systemically elevated in osteoporosis, linking chronic inflammation to skeletal deterioration.

Markers of bone turnover such as C-terminal telopeptide of type I collagen (CTX) and N-terminal telopeptide (NTX) are elevated in both conditions and serve as potential indicators of disease severity. The chronic inflammatory environment also disrupts osteoblast differentiation, favoring apoptosis of bone-forming cells and further impairing bone regeneration [21-24].

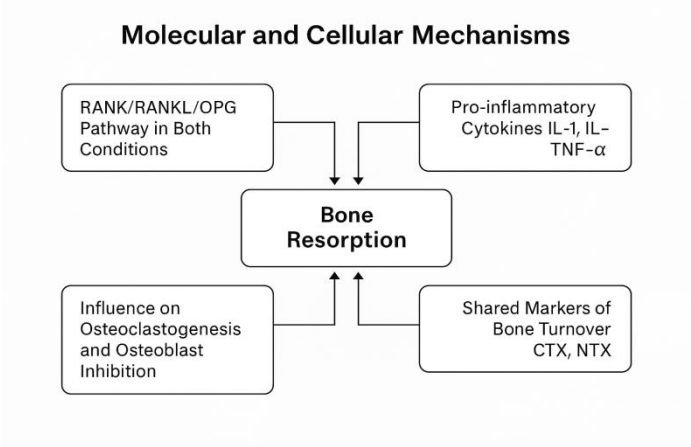

Fig.2: Diagram of the RANK/RANKL/OPG pathway showing its role in osteoclast activation

Table 1: Key Cytokines and Bone Turnover Markers in Periodontitis and Osteoporosis

Molecule	Role	Associated with
RANKL	Stimulates osteoclasts	Both diseases
OPG	Inhibits RANKL	Protective
IL-1, IL-6, TNF-α	Promote inflammation and RANKL	Both diseases
CTX, NTX	Bone resorption markers	Biomarkers for severity

Diagnostic Approaches

Accurate diagnosis of both periodontitis and osteoporosis is crucial for early intervention and prevention of complications. For osteoporosis, Bone Mineral Density (BMD) testing using Dual-energy X-ray Absorptiometry (DEXA) remains the gold standard. A T-score below -2.5 indicates osteoporosis, while -1.0 to -2.5 suggests osteopenia [25].

In periodontitis, diagnosis relies on clinical periodontal indices such as:

- Clinical Attachment Loss (CAL)
- Probing Pocket Depth (PPD)
- Bleeding on Probing (BOP)
- Radiographic assessment of alveolar bone loss

Recent advances include the use of biomarkers in serum and saliva, such as RANKL, OPG, MMPs, and IL-6, for early detection and disease monitoring. These biomarkers provide a non-invasive means to assess both periodontal and systemic bone health.

Table 2: Diagnostic Tools in Periodontitis and Osteoporosis

Condition	Diagnostic Method	Parameters
Osteoporosis	DEXA scan	BMD, T-score
Periodontitis	CAL, PPD, BOP, X-rays	Pocket depth, bone loss
Both	Serum/saliva biomarkers	RANKL, OPG, CTX, NTX, IL-6

Management and Therapeutic Strategies

Managing patients with concurrent periodontitis and osteoporosis requires a comprehensive and multidisciplinary approach [26].

For Osteoporosis

- Anti-resorptive drugs like bisphosphonates (e.g., alendronate) and denosumab reduce osteoclast activity.
- Calcium and vitamin D supplementation helps maintain bone health.
- Hormone replacement therapy (HRT) is considered for postmenopausal women.

For Periodontitis

- Scaling and root planing (SRP) remain the first-line mechanical therapy.
- Adjunctive antimicrobials (e.g., doxycycline) or local drug delivery (e.g., chlorhexidine chips) are often used.
- Anti-inflammatory approaches may include NSAIDs or cytokine blockers under experimental settings.

A multidisciplinary model involving dentists, endocrinologists, and general physicians ensures integrated patient care, minimizing the risk of tooth loss and fractures simultaneously.

Challenges and Limitations

Despite accumulating evidence, several challenges hinder a clear understanding of the periodontitis–osteoporosis connection [27, 28]:

- Confounding variables like age, lifestyle, and medications complicate the interpretation of clinical data.
- Variability in diagnostic criteria for both diseases across studies affects consistency.
- Most clinical studies are cross-sectional or observational, lacking the robustness of long-term randomized trials.
- Adverse effects of anti-resorptive drugs (e.g., medication-related osteonecrosis of the jaw) limit dental intervention options.

Hence, future research must address these limitations with well-designed longitudinal studies that consider these variables.

Future Perspectives

Looking ahead, a few key strategies will help bridge the gaps:

- Development of integrated care models that combine dental and medical services for at-risk populations.
- Identification and validation of novel biomarkers to predict disease onset and progression.
- Focused preventive strategies targeting postmenopausal women and the elderly through education and early screening.
- Application of personalized medicine, including genetic screening and targeted therapy, to manage individuals based on their risk profile.

As the connection between oral and systemic health becomes more evident, interdisciplinary collaboration will play a crucial role in advancing patient care and improving health outcomes.

Conclusion

The relationship between periodontitis and osteoporosis exemplifies a complex, bidirectional interplay involving bone remodeling dysfunction and systemic inflammation. Both conditions, though localized and systemic respectively, share common molecular mediators such as RANKL and pro-inflammatory cytokines, which exacerbate bone resorption. The synergistic impact of these conditions significantly increases the risk of alveolar bone loss, tooth loss, and skeletal fractures, especially in vulnerable populations like postmenopausal women and elderly individuals. The shared risk factors, including estrogen deficiency, calcium and vitamin D insufficiency, smoking, and systemic illnesses like diabetes, further validate the need for combined management strategies. Advances in diagnostics using bone mineral density tests and salivary biomarkers, along with targeted therapeutic interventions such as bisphosphonates, scaling and root planning, and nutritional supplementation, offer a holistic treatment framework. A collaborative approach between dental and medical professionals is essential for identifying at-risk patients, monitoring disease progression, and implementing preventive and therapeutic strategies. Future research must focus on longitudinal studies, development of novel biomarkers, and personalized medicine to improve outcomes.

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Conflict of Interest

Authors are declared that no conflict of interest.

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Polukonda Lakshmi Prasanna, Nallajeru Yamini contributed to literature survey, data compilation, and manuscript drafting. A. Suneetha supported with content organization and technical refinement. Patibandla Jahnavi conceptualized the study, guided the writing process, and approved the final manuscript.

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