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PERIODONTAL DISEASE: MECHANISMS OF PATHOGENESIS – A LITERATURE REVIEW

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Abstract. Periodontal disease is a chronic inflammatory condition affecting the supporting structures of the teeth, including the gingiva, periodontal ligament, cementum, and alveolar bone. It is primarily caused by the accumulation of microbial biofilms on tooth surfaces, leading to host immune responses that can result in progressive tissue destruction. This literature review aims to summarize current knowledge on the etiology and pathogenesis of periodontal disease, highlighting the role of microbial factors, host immune response, genetic predisposition, and environmental influences such as smoking and stress. Understanding the multifactorial nature of periodontal disease is essential for developing targeted preventive and therapeutic strategies.

Keywords: periodontal disease, pathogenesis, inflammation, oral microbiota, host immune response, risk factors, biofilm, gingival inflammation

Introduction. Periodontal disease, encompassing a spectrum of inflammatory conditions affecting the supporting structures of the teeth, stands as a significant global public health concern. Characterized by the progressive destruction of the periodontal ligament and alveolar bone, it often culminates in tooth loss if left untreated. The etiology of periodontal disease is multifactorial, involving complex interactions between pathogenic microorganisms in dental biofilms and the host's immune response [1,5].

Epidemiological data underscore the extensive prevalence of periodontal disease worldwide. According to the Global Burden of Disease Study 2021, over 1 billion individuals were affected by severe periodontitis, with an age-standardized prevalence of 12.5% . Notably, South Asia exhibited the highest prevalence rate at 17.6%. Projections indicate a substantial increase in the burden of severe periodontitis, with estimates suggesting that by 2050, more than 1.5 billion people will be affected, marking a 44.3% rise from 2021 [11].

The pathogenesis of periodontal disease is intricately linked to the host's immune-inflammatory response to microbial colonization. Initial bacterial accumulation triggers an innate immune response, characterized by the recruitment of neutrophils and the release of pro-inflammatory cytokines such as interleukin-1β (IL-1β) and tumor necrosis factor-alpha (TNF-α). These mediators not only orchestrate the inflammatory response but also stimulate the production of matrix metalloproteinases (MMPs), enzymes responsible for the degradation of extracellular matrix components, leading to connective tissue breakdown [12].

Furthermore, the receptor activator of nuclear factor kappa-B ligand (RANKL)/osteoprotegerin (OPG) axis plays a pivotal role in alveolar bone resorption associated with periodontitis [4,12]. An imbalance favoring RANKL promotes osteoclast differentiation and activation, resulting in bone loss. Additionally, emerging evidence

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highlights the contribution of dysbiosis—a disruption in the composition of the oral microbiota—to the chronicity and progression of periodontal disease [14].

Given the complex interplay of microbial, immunological, and environmental factors in periodontal disease pathogenesis, a comprehensive understanding of these mechanisms is essential for the development of effective preventive and therapeutic strategies. This literature review aims to elucidate the current knowledge on the etiopathogenic mechanisms underlying periodontal disease, with a focus on microbial interactions, host immune responses, and the molecular pathways involved in tissue destruction[2, 8].

Periodontal disease, a chronic inflammatory condition affecting the supporting structures of the teeth, has been extensively studied due to its high prevalence and association with systemic health issues. Globally, periodontal diseases affect up to 90% of the population, making them the most common oral diseases [10,14]. In 2021, over 1 billion individuals were affected by severe periodontitis, with an age-standardized prevalence of 12.5% [9,11].

The pathogenesis of periodontal disease involves a complex interplay between microbial biofilms and the host's immune response. The commensal oral bacteria initiate the disease through dysbiosis, leading to an inflammatory response characterized by the release of pro-inflammatory cytokines such as interleukin-1β (IL-1β) and tumor necrosis factor-alpha (TNF-α). These mediators stimulate the production of matrix metalloproteinases (MMPs), enzymes responsible for the degradation of extracellular matrix components, resulting in connective tissue breakdown [14] .

Moreover, the receptor activator of nuclear factor kappa-B ligand (RANKL)/osteoprotegerin (OPG) axis plays a pivotal role in alveolar bone resorption associated with periodontitis. An imbalance favoring RANKL promotes osteoclast differentiation and activation, leading to bone loss.

Several risk factors contribute to the development and progression of periodontal disease. Smoking is a significant modifiable risk factor, with smokers being three times more likely to develop severe periodontitis compared to non-smokers[15]. Diabetes mellitus is another critical risk factor, as it exacerbates the inflammatory response and impairs healing, leading to increased periodontal destruction. Stress, poor oral hygiene, and certain medications also play roles in disease progression.

The association between periodontal disease and systemic conditions has been well-documented. Periodontitis has been linked to cardiovascular diseases, with studies indicating a 19% increased risk of cardiovascular disease in individuals with periodontal disease, and this risk increases to 44% among those aged 65 years and over. Additionally, periodontitis is associated with adverse pregnancy outcomes, respiratory diseases, rheumatoid arthritis, and certain cancers [15].

Methodology.This literature review was conducted to synthesize current knowledge on the pathogenesis of periodontal disease. A comprehensive search of electronic databases, including PubMed, Scopus, and Web of Science, was performed to identify relevant studies published up to April 2025. The search strategy utilized keywords such as "periodontal

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disease," "pathogenesis," "inflammation," "oral microbiota," "host immune response," and "risk factors."

Inclusion criteria encompassed peer-reviewed articles, systematic reviews, meta-analyses, and clinical studies that focused on the mechanisms of periodontal disease development and progression. Studies were selected based on their relevance, methodological rigor, and contribution to understanding the multifactorial nature of periodontal disease.

Data extraction involved summarizing findings related to microbial factors, host immune responses, genetic predispositions, and environmental influences contributing to periodontal disease. Statistical data on prevalence, incidence, and associations with systemic conditions were also collated to provide a comprehensive overview.

The review aimed to integrate current evidence to elucidate the complex interactions underlying periodontal disease pathogenesis, thereby informing future research directions and potential therapeutic strategies.

Results

Global Prevalence and Trends. Periodontal disease remains a significant global health concern, with its prevalence and burden increasing over the past decades. According to the Global Burden of Disease Study 2021, over 1 billion individuals were affected by severe periodontitis, with an age-standardized prevalence of 12.5%. South Asia exhibited the highest prevalence rate at 17.6%. Projections indicate that by 2050, more than 1.5 billion people will be affected, marking a 44.3% rise from 2021[6,7].

The burden of severe periodontitis, measured in Years Lived with Disability (YLDs), was 6.90 million globally in 2021. By 2050, this is expected to increase to 10.06 million YLDs, representing a 43.3% rise. Severe periodontitis is projected to become the 30th most impactful Level 4 disease/condition globally by 2050, moving up one position from its 2021 ranking [11].

Demographic and Risk Factor Associations. The prevalence of periodontal disease increases with age. In the United States, 42.2% of adults aged 30 years or older had periodontitis, with 7.8% having severe periodontitis. Among individuals aged 65 years and older, the prevalence rises to 79.3% [16].

Smoking is a significant modifiable risk factor, accounting for approximately 42% of periodontitis cases. Diabetes mellitus increases the risk of periodontitis approximately three-fold compared to non-diabetic individuals. The combined presence of smoking and diabetes significantly heightens the risk for severe periodontal disease [16].

Immunopathogenic Mechanisms. The pathogenesis of periodontal disease involves a complex interplay between microbial biofilms and the host's immune response. The initial bacterial accumulation triggers an innate immune response, characterized by the recruitment of neutrophils and the release of pro-inflammatory cytokines such as interleukin-1β (IL-1β) and tumor necrosis factor-alpha (TNF-α). These mediators stimulate the production of

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matrix metalloproteinases (MMPs), enzymes responsible for the degradation of extracellular matrix components, leading to connective tissue breakdown.

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Emerging evidence highlights the contribution of inflammasomes, particularly the NLRP3 inflammasome, in periodontal inflammation. Excessive activation of inflammasomes leads to the release of pro-inflammatory cytokines IL-1β and IL-18, contributing to tissue damage. Patients with periodontal pathologies present elevated levels of certain inflammasomes in saliva, proportional to the severity of the disease [17].

Discussion. Periodontal disease remains a significant global health concern, with its prevalence and burden increasing over the past decades. According to the Global Burden of Disease Study 2021, over 1 billion individuals were affected by severe periodontitis, with an age-standardized prevalence of 12.5%. South Asia exhibited the highest prevalence rate at 17.6%. Projections indicate that by 2050, more than 1.5 billion people will be affected, marking a 44.3% rise from 2021.

The pathogenesis of periodontal disease involves a complex interplay between microbial biofilms and the host's immune response. The initial bacterial accumulation triggers an innate immune response, characterized by the recruitment of neutrophils and the release of pro-inflammatory cytokines such as interleukin-1β (IL-1β) and tumor necrosis factor-alpha (TNF-α). These mediators stimulate the production of matrix metalloproteinases (MMPs), enzymes responsible for the degradation of extracellular matrix components, leading to connective tissue breakdown.

The receptor activator of nuclear factor kappa-B ligand (RANKL)/osteoprotegerin (OPG) axis plays a pivotal role in alveolar bone resorption associated with periodontitis. An imbalance favoring RANKL promotes osteoclast differentiation and activation, resulting in bone loss.

Several risk factors contribute to the development and progression of periodontal disease. Smoking is a significant modifiable risk factor, accounting for approximately 42% of periodontitis cases. Diabetes mellitus increases the risk of periodontitis approximately three-fold compared to non-diabetic individuals. The combined presence of smoking and diabetes significantly heightens the risk for severe periodontal disease [17].

The association between periodontal disease and systemic conditions has been well-documented. Periodontitis has been linked to cardiovascular diseases, with studies indicating a 19% increased risk of cardiovascular disease in individuals with periodontal disease, and this risk increases to 44% among those aged 65 years and over. Additionally, periodontitis is associated with adverse pregnancy outcomes, respiratory diseases, rheumatoid arthritis, and certain cancers.

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Emerging evidence highlights the contribution of inflammasomes, particularly the NLRP3 inflammasome, in periodontal inflammation. Excessive activation of inflammasomes leads to the release of pro-inflammatory cytokines IL-1β and IL-18, contributing to tissue damage. Patients with periodontal pathologies present elevated levels of certain inflammasomes in saliva, proportional to the severity of the disease. Given the complex interplay of microbial, immunological, and environmental factors in periodontal disease pathogenesis, a comprehensive understanding of these mechanisms is essential for the development of effective preventive and therapeutic strategies. This literature review aims to elucidate the current knowledge on the etiopathogenic mechanisms underlying periodontal disease, with a focus on microbial interactions, host immune responses, and the molecular pathways involved in tissue destruction.

Conclusion. Periodontal disease is a multifactorial inflammatory condition that results from the complex interplay between microbial dysbiosis, host immune responses, and environmental risk factors. As the most prevalent chronic oral disease globally, affecting over one billion individuals and projected to rise by more than 44% by 2050, its public health implications are substantial.

The pathogenesis involves an orchestrated immune-inflammatory cascade triggered by pathogenic biofilms. Central mediators such as interleukin-1β, tumor necrosis factor-alpha, matrix metalloproteinases, and the RANKL/OPG axis contribute significantly to connective tissue degradation and alveolar bone resorption. Emerging findings on the role of inflammasomes and genetic susceptibility are expanding our understanding of periodontal destruction at the molecular level.

Furthermore, the strong associations between periodontitis and systemic conditions—including cardiovascular disease, diabetes mellitus, and adverse pregnancy outcomes—underscore the importance of periodontal health in systemic disease prevention. Risk factors such as smoking, aging, and metabolic disorders further amplify disease progression and severity.

Given the increasing global burden and systemic relevance of periodontitis, early diagnosis, targeted prevention strategies, and personalized treatment protocols are essential. Future research should prioritize longitudinal and mechanistic studies to refine molecular targets and develop novel therapeutic interventions aimed at modulating both microbial communities and host responses.

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