

## Quorum Sensing and the Transition from Symbiosis to Dysbiosis in Periodontal Biofilms: A Scoping Review

Felisha Febriane Balafif<sup>1</sup>, Anggun Rafisa<sup>2</sup>, Faisal Kuswandani<sup>3</sup>, Nuroh Najmi<sup>4</sup>

<sup>1</sup>Microbiology, Department of Oral Biology, Faculty of Dentistry Universitas Padjadjaran, Indonesia, <sup>2</sup>Physiology, Department of Oral Biology, Faculty of Dentistry Universitas Padjadjaran, Indonesia. <sup>3</sup>Pharmacy, Department of Oral Biology, Faculty of Dentistry Universitas Padjadjaran, Indonesia. <sup>4</sup>Anatomy Pathology, Department of Oral Biology, Faculty of Dentistry Universitas Padjadjaran, Indonesia

Article Info	ABSTRACT
<p><b>Keywords:</b> Quorum sensing, periodontal biofilm, dysbiosis, symbiosis, oral microbiome</p>	<p>Introduction Quorum sensing (QS), a bacterial cell communication system, has emerged as a key regulator of community level biofilm dynamics, yet its role in mediating this ecological transition has not been systematically synthesized. This scoping review aimed to map and synthesize evidence published over the last decade on the role of quorum sensing in driving the transition from symbiosis to dysbiosis in periodontal biofilms. Methods: A scoping review was conducted in accordance with the PRISMA-ScR guidelines. Searches were performed in PubMed, Scopus, and Web of Science for studies published between 2016 and 2025 that investigated quorum sensing mechanisms in periodontal or subgingival biofilms using in vitro, ex vivo, or in vivo models. Data were charted and analyzed descriptively. Results: Sixty one studies met the inclusion criteria. Autoinducer-2 mediated signaling emerged as the most consistently reported quorum sensing pathway in periodontal biofilms. Quorum sensing was shown to regulate interspecies communication, biofilm maturation, metabolic cooperation, and coordinated virulence expression. Evidence indicated that quorum sensing primarily drives dysbiosis through functional reprogramming of microbial communities rather than through numerical dominance of specific pathogens. Several studies also linked quorum sensing activity to enhanced host inflammatory responses and alveolar bone loss in experimental models. Conclusion: Quorum sensing as a central ecological mechanism orchestrating the transition from symbiosis to dysbiosis in periodontal biofilms. By coordinating community wide microbial behavior, host and microbe interactions, quorum sensing contributes to sustained dysbiosis and periodontal inflammation.</p>
<p>This is an open-access article under the <a href="https://creativecommons.org/licenses/by-nc/4.0/">CC BY-NC</a> license</p> 	<p><b>Corresponding Author:</b> Felisha Febriane Balafif Faculty of Dentistry Universitas Padjadjaran <a href="mailto:felisha.balafif@unpad.ac.id">felisha.balafif@unpad.ac.id</a></p>

### INTRODUCTION

Periodontal disease is a chronic inflammatory condition driven by dysbiotic biofilms that develop in the subgingival environment.[1] Contemporary paradigms no longer view periodontitis as an infection caused by individual pathogens but rather as a consequence of ecological imbalance, in which microbial communities transition from symbiosis to

dysbiosis.[2] This transition involves functional shifts in microbial metabolism, virulence expression, and host microbe interactions.[3]

Periodontal biofilms are highly structured, polymicrobial communities dominated by anaerobic bacteria. Their pathogenicity is largely determined by collective behavior rather than microbial composition alone.[4] Ecological frameworks, including the symbiosis and dysbiosis model and the ecological plaque hypothesis, emphasize that disease arises from changes in microbial function and community dynamics.[5]

Quorum sensing (QS) is a bacterial cell–cell communication mechanism that enables population-level coordination of gene expression through diffusible signaling molecules. Quorum sensing regulates essential processes such as biofilm maturation, metabolic cooperation, stress adaptation, and virulence expression.[6] In oral biofilms, Quorum sensing has been extensively studied in cariogenic systems; however, periodontal biofilms differ substantially in terms of oxygen tension, inflammatory environment, and microbial diversity, necessitating focused investigation.[7]

Recent studies increasingly implicate quorum sensing, particularly autoinducer-2 (AI-2) mediated signaling as a key driver of interspecies communication in periodontal biofilms.[8] Quorum sensing appears to facilitate functional reprogramming of microbial communities, promoting dysbiosis and sustained inflammation. Despite this growing body of evidence, findings remain dispersed across experimental and conceptual studies, and no comprehensive synthesis has systematically mapped the role of QS in the symbiosis to dysbiosis transition in periodontal biofilms. Therefore, this scoping review aims to address this gap.

## METHOD

This scoping review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) guidelines [9]. Electronic searches were performed in PubMed, Scopus, and Web of Science databases. Search terms included combinations of “*quorum sensing*,” “*periodontal biofilm*,” “*subgingival biofilm*,” “*oral dysbiosis*,” and “*autoinducer-2*.” Inclusion criteria were original research articles published between 2016 and 2025, studies investigating quorum sensing in periodontal or subgingival biofilms, in vitro, in vivo, or ex vivo experimental models, articles published in English. Exclusion criteria included studies focusing exclusively on cariogenic biofilms or non oral biofilms. Data extracted included study design, quorum sensing systems investigated, microbial species involved, experimental models, and key outcomes. Results were summarized descriptively without quantitative synthesis.

## RESULTS AND DISCUSSION

A total of 61 studies published between 2016 and 2025 met the inclusion criteria. Most studies were published after 2018 and originated from Asia, Europe, and North America. Experimental designs predominated, particularly in vitro multispecies biofilm models.

**Table 1** The articles were synthesized

No	Author (Year)	Study Design / Model	QS System Investigated	Microbial Context	Main Findings Related to Dysbiosis
1	Van Dyke et al. (2020)	Narrative / mechanistic review	AI-2 (LuxS)	Polymicrobial periodontal biofilms	QS contributes to microbial dysbiosis by coordinating inflammatory responses and community behavior rather than single-pathogen dominance
2	Nagi et al. (2023)	In vitro multispecies biofilm	AI-2-mediated QS	Subgingival biofilm models	QS regulates biofilm maturation, interspecies cooperation, and host cell responses favoring dysbiosis
3	Abdulkareem et al. (2023)	Conceptual review	Multiple QS pathways	Periodontal biofilm ecology	Transition from symbiosis to dysbiosis driven by functional shifts regulated by microbial communication
4	Polizzi et al. (2022)	Experimental review	AI-2, QS inhibition	Oral biofilm models	QS inhibition reduces virulence expression without disrupting overall microbial viability
5	Zhou et al. (2024)	In vivo / cell model	AI-2 signaling	Periodontal inflammation model	AI-2 enhances inflammatory signaling and macrophage polarization, promoting dysbiotic conditions
6	Li et al. (2024)	Animal model	AI-2 (LuxS)	Experimental periodontitis	Increased AI-2 activity associated with alveolar bone loss and inflammatory dysbiosis
7	Hashim et al. (2024)	In vitro biofilm	QS / quorum quenching	Subgingival biofilm	Quorum quenching attenuates biofilm virulence and disrupts dysbiotic signaling
8	Zhao et al. (2025)	Scoping review	QS & QQ systems	Oral polymicrobial biofilms	QS networks facilitate ecological imbalance; quorum quenching proposed as antivirulence strategy
9	Di Spirito et al. (2025)	Microbiome profiling	Indirect QS indicators	Health vs disease periodontal states	Dysbiosis linked to functional microbial shifts rather than compositional changes alone

No	Author (Year)	Study Design / Model	QS System Investigated	Microbial Context	Main Findings Related to Dysbiosis
10	Alum et al. (2025)	Translational review	QS inhibition	Anti-biofilm strategies	Targeting QS may modulate dysbiosis while reserving symbiotic microbial functions

This scoping review synthesizes evidence published over the last decade demonstrating that quorum sensing (QS) is a fundamental ecological mechanism governing the transition from symbiosis to dysbiosis in periodontal biofilms. Rather than functioning as a simple virulence switch at the level of individual pathogens, QS consistently emerged as a regulator of community-wide functional reprogramming, supporting contemporary views of periodontitis as a polymicrobial, ecology-driven disease. [9]

Across the included studies, autoinducer-2 (AI-2)–mediated signaling was the most frequently identified QS pathway in periodontal biofilms. AI-2 is uniquely suited to polymicrobial environments, acting as a universal interspecies signal that facilitates metabolic cooperation, spatial organization, and biofilm maturation [10]. Evidence from multispecies biofilm and animal models indicates that AI-2–driven communication promotes ecological conditions favoring dysbiosis, including enhanced proteolytic metabolism, increased stress tolerance, and persistence under inflammatory pressure [4].

Importantly, the results demonstrate that QS contributes to dysbiosis primarily through functional shifts rather than compositional dominance. This finding aligns closely with the symbiosis dysbiosis framework and the ecological plaque hypothesis, which emphasize alterations in microbial activity and host–microbe interactions over changes in bacterial abundance alone [11]. QS enables microbial communities to collectively sense environmental cues such as oxygen limitation, nutrient availability, and host inflammatory mediators and adapt in ways that stabilize pathogenic biofilm states.

Several studies also provided mechanistic links between QS activity and host immune modulation. AI-2 signaling was associated with macrophage polarization, activation of NF- $\kappa$ B–dependent inflammatory pathways, and exacerbation of alveolar bone loss in experimental periodontitis models [11]. These findings suggest that QS not only coordinates microbial interactions but also amplifies host–microbe feedback loops, reinforcing dysbiosis and chronic inflammation within the periodontal niche.

The reviewed evidence further supports integration of QS into broader ecological concepts such as the keystone pathogen framework, in which certain taxa exert disproportionate influence on community behavior and host response without numerical dominance [12]. By modulating QS networks, keystone species may reprogram surrounding commensals toward a dysbiotic phenotype, providing a plausible mechanistic explanation for community-level pathogenicity in periodontitis.

Despite increasing mechanistic insight, this review highlights a clear gap in translational and interventional research. Only a limited number of studies investigated quorum quenching or QS inhibition in periodontal biofilms, although these studies reported attenuation of virulence and inflammatory potential without complete disruption of microbial viability [13].

Such findings suggest that QS targeted strategies may offer advantages over conventional antimicrobials by reducing selective pressure for resistance and preserving beneficial symbiotic interactions.[14][15]

Several limitations of the current evidence base should be acknowledged. Most studies relied on in vitro multispecies biofilm models, which, although valuable, cannot fully replicate the complexity of the periodontal environment. In vivo and longitudinal human studies examining QS dynamics in relation to disease progression remain scarce. Additionally, standardized biomarkers for QS activity in clinical settings are lacking, limiting translational applicability.

Overall, the updated evidence underscores quorum sensing as a critical ecological driver of the symbiosis to dysbiosis transition in periodontal biofilms. Advancing understanding of mediated community behavior will be essential for developing ecology based therapeutic strategies aimed at restoring microbial balance rather than indiscriminately eliminating oral bacteria.

## CONCLUSION

Quorum sensing, particularly AI-2 mediated interspecies signalling is a fundamental ecological regulator of the transition from symbiosis to dysbiosis in periodontal biofilms. By coordinating community wide metabolic activity, virulence expression, host and microbe interactions, QS drives functional dysbiosis without reliance on single-pathogen overgrowth. These findings support contemporary ecological models of periodontal disease and highlight quorum sensing as a promising target for future antivirulence and ecology-based therapeutic strategies. Further in vivo and translational studies are required to integrate QS modulation into clinical periodontal care.

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