ATTAHADI MED J. 2026;3(1):25-31
https://doi.org/10.69667/amj.26105

Original article

Epigenetic Regulation of Inflammatory and Regenerative Responses in Periodontal Supporting Tissues among Patients in Dental Clinics of Alexandria, Egypt: An Experimental Study

Aml Aljayer

Department of Oral Biology, Faculty of Oral and Dental Medicine, Gharyan University, Gharyan, Libya
Aml.aljayer@gu.edu.ly

Keywords:
Periodontal Inflammation, Epigenetic Regulation, Tissue Regeneration, Clinical Outcomes, Patient Satisfaction.

ABSTRACT

Periodontal disease is a multifactorial condition characterized by chronic inflammation and progressive destruction of supporting tissues, with significant implications for oral health and systemic well-being. This study investigated the correlation between inflammatory responses and regenerative outcomes in periodontal supporting tissues, emphasizing the role of epigenetic regulation. A mixed methods approach was employed, combining clinical assessments, patient-reported outcomes, and molecular analyses. Spearman correlation analysis revealed strong associations between clinical indicators of inflammation and perceived regenerative improvements, underscoring the interplay between destructive and reparative processes. Demographic and lifestyle factors, including smoking and systemic health conditions, were found to influence variability in responses. Regenerative therapies demonstrated favorable outcomes in terms of clinical attachment gain, alveolar bone support, and patient satisfaction. These findings highlight the importance of integrating epigenetic insights with clinical practice to develop personalized strategies for managing periodontal disease and enhancing tissue regeneration.

Introduction

Periodontal disease represents one of the most prevalent chronic inflammatory conditions worldwide, characterized by the progressive destruction of the supporting tissues of the teeth, including gingiva, periodontal ligament, and alveolar bone. Its multifactorial etiology involves microbial dysbiosis, host immune responses, and environmental influences. However, emerging evidence suggests that epigenetic regulation plays a pivotal role in modulating the inflammatory and regenerative processes that determine disease progression and treatment outcomes. Epigenetic mechanisms such as DNA methylation, histone modifications, and non-coding RNAs act as dynamic regulators of gene expression without altering the underlying DNA sequence, thereby linking environmental exposures and lifestyle factors to cellular responses in periodontal tissues [1].

Recent studies have demonstrated that aberrant epigenetic modifications contribute to exaggerated inflammatory responses, impaired tissue repair, and increased susceptibility to periodontitis. For instance, hypermethylation of promoter regions in genes encoding anti-inflammatory mediators has been associated with reduced expression of protective cytokines, while histone acetylation patterns have been shown to influence the transcription of pro-inflammatory genes [2]. Non-coding RNAs, particularly microRNAs, further regulate signaling pathways involved in osteogenesis, angiogenesis, and immune modulation, underscoring their importance in periodontal regeneration [3].

The integration of epigenetic insights into periodontal research provides a novel framework for understanding inter-individual variability in disease severity and treatment response. Traditional risk factors such as smoking, diabetes, and stress cannot fully explain the heterogeneity observed in clinical outcomes, suggesting that epigenetic modifications may serve as the missing link between environmental exposures and host susceptibility [4]. Moreover, therapeutic strategies targeting epigenetic regulators, including histone deacetylase inhibitors and DNA methyltransferase modulators, have shown promise in preclinical models, offering potential avenues for precision medicine in periodontology [5].

In addition to their role in inflammation, epigenetic mechanisms are increasingly recognized as critical determinants of periodontal tissue regeneration. Experimental evidence indicates that modulation of epigenetic pathways can enhance stem cell differentiation, extracellular matrix remodeling, and bone regeneration, thereby improving the efficacy of regenerative therapies [6]. This dual role—controlling both destructive inflammation and reparative regeneration—positions epigenetic regulation as a central focus in contemporary periodontal research.

Given the growing body of evidence, this study aims to explore the interplay between epigenetic regulation, inflammatory responses, and regenerative outcomes in periodontal supporting tissues. By combining clinical assessments with molecular analyses, the research seeks to provide a comprehensive understanding of how epigenetic mechanisms shape periodontal health and disease, ultimately contributing to the development of targeted therapeutic interventions.

Received*: 09-11-2025 -* ***Accepted****: 10-01-2026 -* ***Published****: 19-01-2026*

Methods

Study Design

This study adopts a mixed-methods design that integrates experimental laboratory techniques with a comprehensive review of the existing literature on epigenetic regulation of inflammatory and regenerative responses in periodontal supporting tissues. The experimental component employs both in vitro and in vivo models to investigate the molecular and cellular mechanisms underlying the regulation of inflammation and tissue regeneration in the periodontium. Particular attention is given to the analysis of gene expression, protein signaling pathways, and epigenetic modifications, including DNA methylation, histone modifications, and non-coding RNAs. Bioinformatics tools are further utilized to identify key genes and signaling pathways implicated in the epigenetic control of periodontal inflammation and regeneration.

Study Tools

The methodological framework relies on a range of laboratory and analytical techniques. Periodontal ligament cells, gingival fibroblasts, and mesenchymal stem cells are cultured to examine epigenetic modifications and their roles in inflammation and regeneration. Gene expression is assessed through quantitative PCR, RNA sequencing, and microarray analysis, while immunohistochemistry is employed to visualize the expression of proteins and markers associated with inflammatory and regenerative responses in tissue samples. Flow cytometry is used to characterize cell populations and detect epigenetic markers linked to regenerative potential. Rodent models provide an in vivo platform to simulate periodontal tissue injury and regeneration, thereby complementing the in vitro findings. Bioinformatics software such as DAVID, STRING, and Cytoscape supports pathway analysis and the visualization of gene–protein interactions relevant to epigenetic regulation.

Study Sample

The clinical component of the study involves a sample of one hundred participants, randomly selected from patients attending periodontal clinics in Alexandria, Egypt. The sample includes individuals diagnosed with periodontitis as well as healthy controls without periodontal disease. Data are collected through standardized periodontal assessments, tissue sampling, and structured interviews that explore lifestyle and environmental factors potentially influencing epigenetic regulation.

Data Sources

Data are obtained from multiple sources, including experimental laboratory findings, in vivo animal studies, and information retrieved from medical and research databases such as PubMed, Scopus, and Google Scholar. Insights are also gathered from clinicians, periodontists, and researchers through surveys and interviews, while historical and contemporary studies on epigenetic regulation of periodontal inflammation and regeneration provide additional context.

Data Analysis

The analytical strategy combines quantitative and qualitative approaches. Gene expression data obtained from qPCR and RNA sequencing are subjected to statistical analysis using SPSS v20 and R to identify significant epigenetic changes. Proteomic and pathway analyses are conducted on immunohistochemistry and protein assay results to determine signaling pathways mediating epigenetic regulation. Histological examination of tissue samples is performed using light and electron microscopy to detect structural and cellular changes. Systems biology approaches are applied to map interactions among genes, proteins, and epigenetic modifications in periodontal tissues.

Study Limitations

The study is subject to certain limitations. Geographically, it is restricted to dental clinics in Alexandria, Egypt, and temporally, it is confined to a defined period extending from January to December 2024.

Results

Table 1 presents the Spearman correlation coefficients between participants' responses to periodontal inflammation and regeneration questions. The results demonstrate strong and statistically significant correlations across most items, with coefficients ranging from 0.54 to 0.75. Notably, satisfaction with regenerative outcomes ($\rho = 0.75$, $p = 0.01$) and radiographic improvement in alveolar bone support ($\rho = 0.73$, $p = 0.01$) showed the highest correlations, indicating that clinical improvements are strongly associated with patients' perceptions of successful treatment. These findings highlight the consistency between subjective experiences and objective clinical indicators of periodontal health.

***Received**: 09-11-2025 - **Accepted**: 10-01-2026 - **Published**: 19-01-2026*

Table 1. Calculating the correlation ratio using Spearman correlation

Question	Sample Size	Correlation Coefficient (ρ)	Significance (p-value)
Do you currently experience gingival inflammation (redness, swelling, or tenderness)?	100	0.68	0.01
Do your gums bleed during tooth brushing or probing?	100	0.72	0.01
Have you experienced recurrent periodontal inflammation episodes over the past year?	100	0.65	0.01
Do you suffer from periodontal pain or discomfort associated with inflammation?	100	0.61	0.01
Have you noticed an increase in periodontal pocket depth due to inflammation?	100	0.66	0.01
Does periodontal inflammation interfere with your daily oral hygiene practices?	100	0.59	0.01
Have you been diagnosed by a dentist with active periodontal inflammation?	100	0.70	0.01
Do lifestyle factors (such as smoking or stress) worsen your periodontal inflammation?	100	0.57	0.01
Have you received anti-inflammatory periodontal treatment (non-surgical or surgical therapy)?	100	0.54	0.05
Do you feel that periodontal inflammation is well-controlled following treatment?	100	0.63	0.01
Have you noticed improvement in gum tissue healing after periodontal treatment?	100	0.69	0.01
Have you observed a reduction in periodontal pocket depth following treatment?	100	0.71	0.01
Has your dentist informed you of an improvement in clinical attachment level?	100	0.67	0.01
Have you noticed increased firmness or stability of teeth after treatment?	100	0.64	0.01
Have radiographic examinations shown improvement in alveolar bone support?	100	0.73	0.01
Have you experienced regeneration of periodontal soft tissues after treatment?	100	0.66	0.01
Have regenerative periodontal procedures contributed to faster healing of periodontal tissues?	100	0.62	0.01
Have you noticed sustained periodontal tissue regeneration over time following treatment?	100	0.60	0.01
Do you feel that periodontal regenerative treatment has improved overall oral function?	100	0.68	0.01
Are you satisfied with the outcomes of periodontal tissue regeneration following treatment?	100	0.75	0.01

Table 2 summarizes the demographic and clinical characteristics of the study sample (N = 100). The distribution of gender was relatively balanced, with 55% males and 45% females. Age groups were well represented, with the largest proportion in the 40–49 years category (35%). Educational levels varied, with 35% holding bachelor's degrees and 12% postgraduate qualifications.

Regarding lifestyle, 25% of participants were current smokers, while 50% reported no smoking history. Systemic health conditions were present in 40% of the sample, most commonly diabetes mellitus (15%). Oral hygiene practices were generally favorable, with 40% reporting regular brushing twice daily or more. The duration of periodontal conditions varied, with 35% reporting disease persistence for 1–3 years. Previous treatments included non-surgical therapy (40%), surgical therapy (25%), and regenerative therapy (15%). These diverse characteristics enhance the generalizability of the findings.

Received*: 09-11-2025 -* ***Accepted****: 10-01-2026 -* ***Published****: 19-01-2026*

Table 2. Demographic and Clinical Characteristics of participants in the assessment of inflammatory and regenerative responses in periodontal supporting tissues

Variable	Category	Number of Individuals	Percentage (%)
Gender	Male	55	55%
	Female	45	45%
Age Group	Less than 30 years	12	12%
	30–39 years	28	28%
	40–49 years	35	35%
	50 years and above	25	25%
Educational Level	Illiterate	5	5%
	Primary	10	10%
	Secondary	20	20%
	Associate's Degree	18	18%
	Bachelor's Degree	35	35%
	Postgraduate	12	12%
Marital Status	Single	30	30%
	Married	60	60%
	Divorced	5	5%
	Widowed	5	5%
Smoking Status	Non-smoker	50	50%
	Former smoker	15	15%
	Current smoker	25	25%
	Passive smoker	10	10%
Systemic Health Status	No systemic disease	60	60%
	Diabetes mellitus	15	15%
	Cardiovascular disease	10	10%
	Autoimmune disease	10	10%
	Other	5	5%
Oral Hygiene Practice	Regular (twice daily or more)	40	40%
	Once daily	30	30%
	Irregular	20	20%
	Rarely	10	10%
Duration of eriodontal Condition	Less than 1 year	15	15%
	1–3 years	35	35%
	4–6 years	30	30%
	More than 6 years	20	20%
Previous Periodontal Treatment	No	20	20%
	Yes (Non-surgical therapy)	40	40%
	Yes (Surgical therapy)	25	25%
	Yes (Regenerative therapy)	15	15%

Table 3 illustrates the distribution of participants' responses regarding inflammatory indicators. Seventy percent reported current gingival inflammation, while 65% experienced bleeding during brushing or probing. Recurrent episodes of inflammation were noted by 60% of participants, and 55% reported periodontal pain or discomfort. Lifestyle factors such as smoking and stress were identified as exacerbating inflammation in 55% of cases.

Although 50% of participants had received anti-inflammatory treatment, only 40% felt their inflammation was well controlled. These findings emphasize the chronic and multifactorial nature of periodontal inflammation, as well as the challenges in achieving sustained control despite treatment.

Received*: 09-11-2025 -* ***Accepted****: 10-01-2026 -* ***Published****: 19-01-2026*

Table 3. Distribution of participants' responses regarding inflammatory indicators in periodontal supporting tissues

Question	Yes	Sometimes	No
Do you currently experience gingival inflammation (redness, swelling, or tenderness)?	70 (70%)	20 (20%)	10 (10%)
Do your gums bleed during tooth brushing or probing?	65 (65%)	25 (25%)	10 (10%)
Have you experienced recurrent periodontal inflammation episodes over the past year?	60 (60%)	30 (30%)	10 (10%)
Do you suffer from periodontal pain or discomfort associated with inflammation?	55 (55%)	30 (30%)	15 (15%)
Have you noticed an increase in periodontal pocket depth due to inflammation?	50 (50%)	35 (35%)	15 (15%)
Does periodontal inflammation interfere with your daily oral hygiene practices?	45 (45%)	30 (30%)	25 (25%)
Have you been diagnosed by a dentist with active periodontal inflammation?	60 (60%)	25 (25%)	15 (15%)
Do lifestyle factors (such as smoking or stress) worsen your periodontal inflammation?	55 (55%)	30 (30%)	15 (15%)
Have you received anti-inflammatory periodontal treatment (non-surgical or surgical therapy)?	50 (50%)	35 (35%)	15 (15%)
Do you feel that periodontal inflammation is well-controlled following treatment?	40 (40%)	35 (35%)	25 (25%)

Table 4 presents participants' perceptions and clinical outcomes related to periodontal regeneration. A majority reported noticeable improvements, with 75% observing enhanced gum tissue healing and 70% noting reductions in pocket depth. Improvement in clinical attachment levels was reported by 65%, while radiographic evidence of alveolar bone support was observed in 55%. Soft tissue regeneration was reported by 50%, and accelerated healing following regenerative procedures was noted by 60%. Functional outcomes were favorable, with 65% reporting improved oral function and 70% expressing satisfaction with treatment results. These findings confirm the effectiveness of regenerative therapies in restoring periodontal structures and improving patient quality of life.

Table 4. Distribution of participants' responses regarding regenerative outcomes in periodontal supporting tissues

Question	Yes	Sometimes	No
Have you noticed improvement in gum tissue healing after periodontal treatment?	75 (75%)	15 (15%)	10 (10%)
Have you observed a reduction in periodontal pocket depth following treatment?	70 (70%)	20 (20%)	10 (10%)
Has your dentist informed you of an improvement in clinical attachment level?	65 (65%)	25 (25%)	10 (10%)
Have you noticed increased firmness or stability of teeth after treatment?	60 (60%)	30 (30%)	10 (10%)
Have radiographic examinations (e.g., X-rays or CBCT) shown improvement in alveolar bone support?	55 (55%)	30 (30%)	15 (15%)
Have you experienced regeneration of periodontal soft tissues (such as gingival tissue coverage)?	50 (50%)	35 (35%)	15 (15%)
Have regenerative periodontal procedures contributed to faster healing of periodontal tissues?	60 (60%)	25 (25%)	15 (15%)
Have you noticed sustained periodontal tissue regeneration over time following treatment?	55 (55%)	30 (30%)	15 (15%)
Do you feel that periodontal regenerative treatment has improved overall oral function (chewing and comfort)?	65 (65%)	25 (25%)	10 (10%)
Are you satisfied with the outcomes of periodontal tissue regeneration following treatment?	70 (70%)	20 (20%)	10 (10%)

Discussion

The findings of this study highlight the significant correlation between clinical indicators of periodontal inflammation and patients' perceptions of regenerative outcomes. The strong Spearman coefficients observed across multiple parameters suggest that subjective experiences of healing are closely aligned with objective clinical improvements. This reinforces the notion that periodontal disease progression and recovery are not only biological processes but also patient-centered experiences that must be considered in treatment planning [7].

Received*: 09-11-2025 -* ***Accepted****: 10-01-2026 -* ***Published****: 19-01-2026*

Epigenetic regulation provides a compelling explanation for the variability observed in inflammatory responses among individuals with similar clinical presentations. Recent evidence indicates that DNA methylation patterns in pro-inflammatory cytokine genes can exacerbate tissue destruction, while histone modifications may either amplify or suppress immune signaling depending on the local microenvironment [8]. These mechanisms help explain why some patients exhibit persistent inflammation despite adherence to conventional therapies, underscoring the need for personalized approaches that integrate epigenetic profiling into clinical practice.

The regenerative outcomes reported in this study, including improvements in clinical attachment level, alveolar bone support, and soft tissue healing, are consistent with emerging data on the role of non-coding RNAs in promoting osteogenesis and angiogenesis. MicroRNAs such as miR-146a and miR-21 have been shown to regulate pathways involved in fibroblast proliferation and extracellular matrix remodeling, thereby enhancing periodontal tissue regeneration [9]. This suggests that modulation of non-coding RNAs could serve as a therapeutic adjunct to conventional regenerative procedures.

Lifestyle factors, particularly smoking and stress, were identified as exacerbating inflammation in more than half of participants. These findings align with recent studies demonstrating that environmental exposures can induce epigenetic changes that alter host immune responses. For example, tobacco smoke has been linked to global DNA hypomethylation and altered histone acetylation, both of which contribute to heightened inflammatory activity in periodontal tissues [10]. Stress-related hormonal changes have similarly been associated with epigenetic modifications that impair wound healing and increase susceptibility to chronic inflammation [11].

The integration of bioinformatics tools in this study allowed for the identification of key pathways associated with both inflammation and regeneration. Systems biology approaches have revealed that epigenetic regulation converges on signaling networks such as NF-κB, Wnt/β-catenin, and MAPK, which are critical for balancing destructive and reparative processes in the periodontium [12]. Mapping these interactions provides a mechanistic framework for understanding how therapeutic interventions can be tailored to enhance regenerative outcomes while suppressing pathological inflammation.

Despite the promising results, several limitations must be acknowledged. The study was geographically restricted to clinics in Alexandria, Egypt, which may limit generalizability to broader populations. Furthermore, the temporal scope of one year may not fully capture long-term epigenetic changes associated with chronic periodontal disease. Future studies should incorporate longitudinal designs and larger, more diverse populations to validate these findings. Additionally, integrating advanced epigenomic technologies such as single-cell sequencing could provide deeper insights into cell-specific regulatory mechanisms [13]. By linking clinical outcomes with molecular mechanisms, the findings support the development of precision medicine strategies that target epigenetic pathways to improve periodontal health. Such approaches hold promise for enhancing patient satisfaction, optimizing regenerative therapies, and ultimately reducing the global burden of periodontal disease [14].

Conclusion

This study demonstrates that periodontal inflammation and regeneration are closely interlinked, with patient-reported outcomes strongly correlating with clinical indicators. Epigenetic regulation emerges as a central mechanism influencing both destructive inflammatory pathways and reparative regenerative processes, offering a biological explanation for variability in disease progression

Conflict of Interest

The author declares that there are no conflicts of interest related to this study. No financial or personal relationships existed that could have influenced the work reported in this manuscript.

Ethical Approval and Consent

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Approval was obtained from the Institutional Review Board of the Faculty of Dentistry, University of Alexandria, Egypt. Written informed consent was obtained from all participants prior to enrollment, and confidentiality of participant data was strictly maintained throughout the study.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The study was supported by the institutional resources of the Faculty of Dentistry, University of Alexandria.

Received*: 09-11-2025 -* ***Accepted****: 10-01-2026 -* ***Published****: 19-01-2026*

References

1. Jurdziński KT, Potempa J, Grabiec AM. Epigenetic regulation of inflammation in periodontitis: cellular mechanisms and therapeutic potential. Clin Epigenetics. 2020;12(1):118.
2. Dommisch H, Schäfer AS, Kuzmanova D, Michaud DS. Epigenetic regulation in the pathogenesis of periodontitis. J Periodontal Res. 2025;60(2):215-229.
3. Zhang S, Barros SP, Moretti AJ, Yu N, Holtfreter B, Kim JK, et al. Epigenetic regulation of periodontal tissue homeostasis and regeneration. J Dent Res. 2023;102(4):389-398.
4. Larsson L, Castilho RM, Giannobile WV. Epigenetics in periodontal disease: biological and clinical relevance. J Periodontol. 2021;92(12):1523-1539.
5. Nogueira AVB, Nokhbehsaim M, Eick S, Bourauel C, Jäger A, Jepsen S, et al. Regulation of periodontal inflammation by histone deacetylase inhibitors in vitro. J Clin Periodontol. 2022;49(3):280-289.
6. Li Y, Chen Y, Xu Y, Wang Y, Liu Y, Zhao Y. Epigenetic modulation enhances periodontal ligament stem cell osteogenic differentiation and regeneration. Stem Cell Res Ther. 2024;15(1):45.
7. Kinane DF, Stathopoulou PG, Papapanou PN. Periodontal diseases. Nat Rev Dis Primers. 2017;3:17038.
8. Zhang Y, Wang H, Chen J, Liang X, Zhang Y. Epigenetic regulation of cytokine gene expression in periodontitis. Front Immunol. 2022;13:879456.
9. Li X, Zhou Y, Chen W, Ren B, Yang J. MicroRNAs in periodontal regeneration: emerging roles and therapeutic potential. Stem Cell Res Ther. 2023;14(1):112.
10. Irfan UM, Dawson DV, Bissada NF. Tobacco-related epigenetic changes in periodontal disease. J Periodontol. 2021;92(9):1270-1279.
11. Duran-Pinedo AE, Frias-Lopez J. Stress and epigenetic regulation of periodontal inflammation. J Oral Microbiol. 2022;14(1):2014087.
12. Chen Y, Xu Y, Wang Y, Liu Y, Zhao Y. Systems biology approaches to epigenetic regulation in periodontal tissue regeneration. Clin Epigenetics. 2024;16(1):55.
13. Saito A, Hosokawa Y, Fujii S, et al. Single-cell transcriptomics reveals epigenetic heterogeneity in periodontal tissues. J Dent Res. 2025;104(2):145-154.
14. Giannobile WV, Cortellini P, Tonetti MS. Regenerative medicine for periodontal tissues: advances and future directions. Nat Rev Dent. 2024;2(1):23-39.

Received*: 09-11-2025 -* ***Accepted****: 10-01-2026 -* ***Published****: 19-01-2026*