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Biological Markers to Detect Periodontal Severity in Postmenopausal Women: A Systematic Review

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ABSTRACT

Periodontal disease is a significant health concern, particularly in postmenopausal women due to hormonal changes affecting immune response and bone metabolism. This study reviews non-invasive biomarkers for detecting and monitoring disease severity through a literature search in PubMed, Cochrane Library, and Science Direct (2015–2025). Five studies found that biomarkers such as salivary cytokines, calcium, estradiol, calprotectin, and serum markers are significantly associated with periodontal clinical parameters. These biomarkers show potential for early detection and personalized management, although further research is still needed.

Keyword: Periodontitis, Biomarkers, Postmenopausal Women, Saliva, Inflammatory Cytokines, Systematic Review.

ABSTRAK

Penyakit periodontal merupakan masalah kesehatan yang signifikan, terutama pada wanita pascamenopause akibat perubahan hormonal yang memengaruhi sistem imun dan metabolisme tulang. Studi ini meninjau biomarker non-invasif untuk deteksi dan pemantauan keparahan penyakit periodontal melalui pencarian literatur pada PubMed, Cochrane Library, dan Science Direct (2015–2025). Lima studi menunjukkan bahwa biomarker seperti sitokin saliva, kalsium, estradiol, kalprotektin, serta penanda serum memiliki hubungan signifikan dengan parameter klinis periodontal. Biomarker berpotensi sebagai alat deteksi dini dan manajemen personal, namun masih diperlukan penelitian lanjutan.

Kata kunci: Periodontitis, Biomarker, Wanita pascamenopause, Saliva, Sitokin inflamasi, Tinjauan sistematis.

1. Introduction

Periodontal disease is a prevalent chronic inflammatory condition affecting the supporting structures of the teeth, with significant implications for oral and systemic health. Globally, it remains a leading cause of tooth loss in adults, with recent data estimating that the disease affects approximately 50% of the world's population, making it the sixth most prevalent disease worldwide.[1] The burden of periodontitis is particularly significant in aging populations, including postmenopausal women, where risk factors, such as hormonal changes, systemic comorbidities, and immunosenescence, increase susceptibility and severity.[2] Therefore, understanding the unique risk profile of postmenopausal women is essential for effective prevention, early detection, and management.

Menopause is characterized by a decline in estrogen production, which exerts profound effects on both oral and systemic health. Estrogen receptors are present in the oral mucosa, gingiva, and periodontal ligament, implicating hormonal changes in the modulation of local immune response, vascularity, and bone metabolism.[3] The reduction in the hormone accelerates bone resorption, increases gingival inflammation, and alters the host response to bacterial challenge, thereby heightening the risk and progression of periodontitis.[4] Several epidemiological studies have confirmed a higher prevalence and severity of periodontal disease in postmenopausal women, indicating the importance of targeted diagnostic and therapeutic approaches in this population.[5]

Traditional clinical assessments of periodontal disease, such as probing depth, clinical attachment level, and radiographic bone loss, provide valuable information but are inherently limited by their inability to reflect current disease activity and early pathophysiological changes.[6] These parameters are retrospective in nature and may fail to capture the dynamic aspects of inflammation and tissue breakdown. This indicates an urgent need for objective, sensitive, and non-invasive tools to monitor periodontal status, particularly in populations with unique risk profiles.[7]

Biological markers, or biomarkers, have emerged as promising adjuncts in the diagnosis and monitoring of periodontal disease. Salivary and gingival crevicular fluid (GCF) biomarkers can provide real-time insights into the host's inflammatory status, microbial challenge, and tissue destruction.[8] Advances in proteomics, genomics, and metabolomics have also enabled the identification of a wide array of candidate biomarkers, including cytokines, matrix metalloproteinases, acute-phase proteins, and bone turnover markers, that reflect various aspects of periodontal pathogenesis.[9] The non-invasive nature of saliva and GCF collection makes these fluids especially attractive for large-scale screening, longitudinal monitoring, and individualized risk assessment in clinical practice.[10]

Recent studies have shown the potential value of inflammatory cytokines, such as interleukin-1β (IL-1β), tumor necrosis factor-α (TNF-α), and matrix metalloproteinase-8 (MMP-8) as diagnostic and prognostic biomarkers for periodontal disease in postmenopausal women.[11] Changes in the levels of these mediators have been shown to correlate with both clinical parameters and disease progression, reflecting the impact of hormonal status on local inflammatory responses.[12] In addition, systemic markers of bone turnover, such as osteoprotegerin and neopterin, are increasingly recognized as important indicators of periodontal breakdown in women experiencing estrogen deficiency.[13]

In addition to cytokines and protein markers, salivary steroid hormones, including estradiol and its metabolites, have been investigated as potential biomarkers linking menopause and periodontal disease.[14] Declining salivary estradiol has been associated with increased attachment loss, higher plaque accumulation, and xerostomia, further substantiating the interplay in postmenopausal women.[15] The integration of multiple biomarker classes, comprising inflammatory, bone, and hormonal mediators, may enhance the specificity and sensitivity of diagnostic algorithms and facilitate precision dentistry.

Despite the growing body of studies supporting the use of biomarkers in periodontal diagnostics, important gaps remain regarding their standardization, validation, and clinical implementation.[16] Variability in study design, assay methods, and population characteristics complicates the interpretation and generalizability of results. Few studies have also specifically focused on postmenopausal women, indicating the need for systematic evaluation of existing evidence to inform tailored clinical decision-making in this high-risk group.[17] Therefore, this study aims to systematically review current evidence

on biological markers for detecting periodontal severity in postmenopausal women. By obtaining data from recent observational studies, the study identifies the most promising salivary, crevicular, and serum biomarkers for risk assessment, disease monitoring, and prognostic evaluation. The results are expected to contribute to the development of non-invasive, patient-centered diagnostic strategies that address the unique needs of postmenopausal women and improve periodontal health outcomes.[18]

2. Methods

2.1. Protocol and Registration

This systematic review was registered on PROSPERO in August 2025, with registration number: CRD420251130274. No amendments to this registration were made.

2.2. Eligibility Criteria

The systematic review included original study articles that investigated the association between biological markers and periodontal disease severity in postmenopausal women without any intervention. Only studies with clear definitions of both postmenopausal status and periodontal outcomes were included. Eligible study designs comprised observational studies such as cross-sectional, case-control, and cohort studies, as well as clinical trials including human participants. Articles had to report at least one biological marker (including but not limited to cytokines, hormones, or bone turnover markers) measured in relevant biological fluids or tissues. Publications were restricted to the English language and to those published between August 2015 and August 2025. Exclusion criteria were review articles, conference abstracts, case reports, editorials, animal studies, in vitro studies, and studies not specifically focusing on postmenopausal populations.

2.3. Information Sources and Search Strategy

A comprehensive literature search was performed using PubMed, Cochrane Library, and Science Direct, covering articles published up until 18th of August 2025. The search strategy combined both Medical Subject Headings (MeSH) and free-text keywords related to periodontal disease, postmenopausal women, and several biological markers. The search terms included: ‘periodontitis’, ‘periodontal disease’, ‘menopause’, ‘postmenopausal’, ‘biomarkers’, ‘cytokines’, ‘IL-1β’, ‘TNF-α’, ‘estradiol’, ‘MMP-8’, ‘calcium’, ‘albumin’, and ‘osteoprotegerin’, together with sample-related terms such as ‘saliva’, ‘gingival crevicular fluid’, ‘GCF’, ‘serum’, and ‘plasma’. Reference lists of relevant studies and reviews were also screened to identify additional articles.

2.4. Study Selection

All records retrieved from the database searches were imported into reference management software, and duplicates were removed. In this study, 2 reviewers independently screened the titles and abstracts of all studies for relevance to the review question. Full-text articles of potentially eligible studies were then retrieved and assessed against the predetermined inclusion and exclusion criteria. Any disagreements between reviewers were resolved by discussion. The selection process was documented in accordance with PRISMA guidelines, including reasons for exclusion at the full-text stage.

2.5. Data Extraction

Data extraction was performed independently by 2 reviewers using a standardized data extraction form. Information collected included the first author’s name, publication year, study design, sample size, population characteristics, main clinical or periodontal parameters, the specific biomarkers assessed, type of biological sample analyzed (such as saliva, serum, gingival crevicular fluid, or urine), and the main conclusions of the study. For studies with multiple groups or biomarkers, all relevant subgroup data were extracted.

2.6. Quality Assessment

The methodological quality and risk of bias for each included study were independently assessed by 2 reviewers. Cross sectional and case-control study was evaluated using the Joanna Briggs Institute (JBI) Critical Appraisal tools. Any discrepancies in quality ratings were resolved by discussion. The overall risk of bias and quality ratings were incorporated into the data synthesis and interpretation of results.

2.7. Data Synthesis and Analysis

Due to the expected heterogeneity in study designs, types of biomarkers, assay techniques, and outcome measures, a meta-analysis was not conducted. Instead, data from the included studies were synthesized descriptively and presented in detailed summary tables. The results were discussed in the context of methodological quality, biomarker categories, and clinical significance. Remaining gaps in the literature and implications for future study and clinical practice were also emphasized.

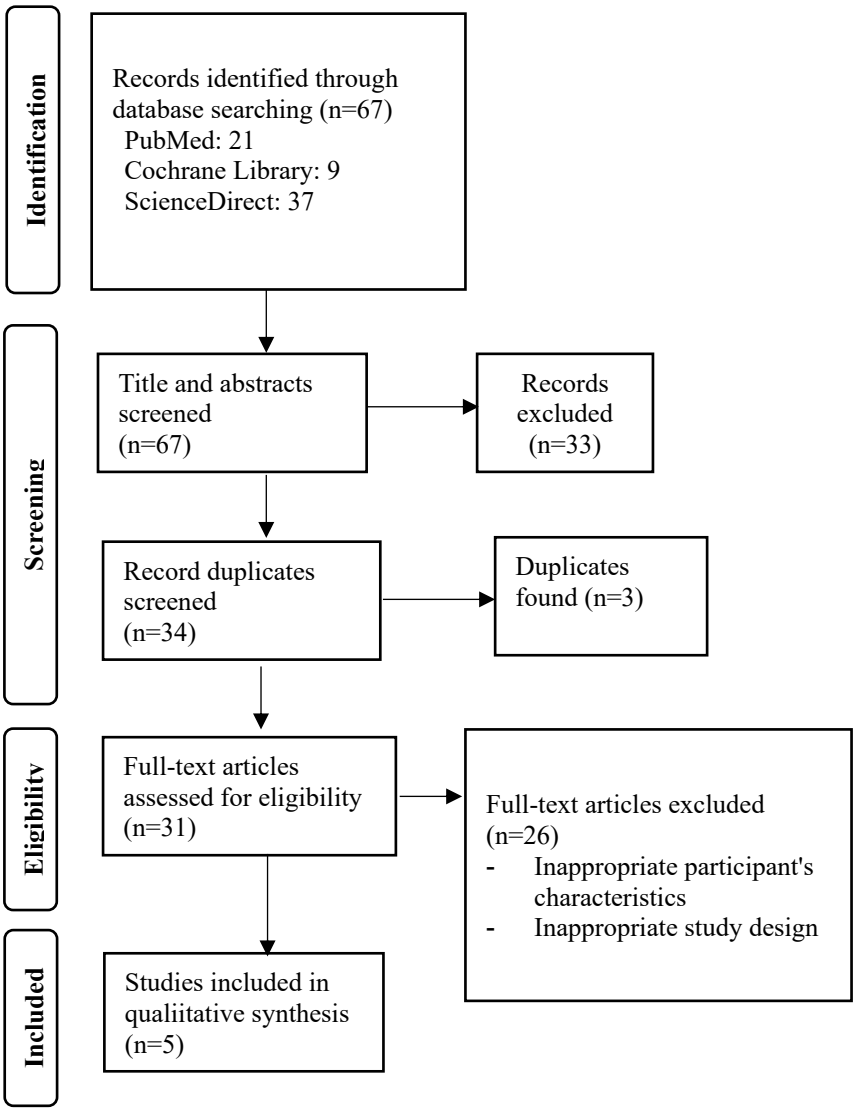

Figure 1. Diagram flow of literature search strategy for this systematic review

Table 1. Characteristics and results of the included studies

Study (Author, Year)	Country	Design	Population	n	Main Biomarker(s)	Main Findings / Summary
Pavitra, 2024[19]	India	Cross-sectional evaluative study	Post-menopause women with periodontitis	12	Bone Mineral Density (BMD) and Salivary Calcitonin	A statistically significant difference in salivary calprotectin levels was seen between groups 1 and 2 (P = 0.016), although no statistical difference in mean bone mineral density levels was noted between the two groups (P = 0.235).
			Post-menopause women without periodontitis	12		
Hutomo, 2021[20]	Indonesia	Cross-sectional	Healthy post-menopausal women	49	Serum ALP and serum calcium	Serum ALP exhibited a strong correlation with the severity of periodontitis, clinical attachment loss, and tooth loss in perimenopausal and postmenopausal women ($p < 0.05$). Serum calcium levels had no correlation with periodontal status.
			Healthy perimenopausal women	22		
Potdar, 2023[21]	India	Cross-sectional	Post-menopause women with periodontitis	26	Salivary IL-8 and Calcium level	A statistical difference in salivary IL-8 levels was observed between two groups, with no significant difference in calcium levels. A weak negative association was observed in group I, while a weak positive correlation was identified in group II.
			Post-menopause women without periodontitis	26		
Soundarya, 2022[5]	India	Cross-sectional	Healthy menstruating women	20	Salivary estradiol and salivary calcium level	Postmenopausal women exhibited low salivary estradiol levels and elevated salivary calcium levels; furthermore, a decline in salivary estradiol correlated with an increase in xerostomia scores and salivary calcium levels. Moreover, as salivary calcium levels rose, the scores for periodontal disease likewise escalated. All parameters were within normal ranges in healthy menstrual women.
			Premenopausal women	20		
			Menopausal women	20		
Agrawal, 2018[22]	India	Case-control	Premenopausal women with periodontitis	20	Salivary TNF-α	Salivary concentrations of TNF-α were elevated in both menopause and chronic periodontitis. The elevated secretion of TNF-α may have a role in the advancement of periodontal disease in post-menopausal women, indicating that salivary TNF-α could serve as a possible biomarker and a useful adjunct for the screening of periodontal disease in this demographic.
			Postmenopausal women with periodontitis	20		
			Premenopausal women without periodontitis	20		
			Postmenopausal women without periodontitis	20		

Table 2. Risk of bias results

Author	Score based on appropriate JBI appraisal for cross sectional studies										Overall appraisal
	1	2	3	4	5	6	7	8			
Pavithra, 2024	Y	Y	Y	Y	Y	N	Y	Y			Included
Hutomo, 2021	Y	Y	Y	Y	Y	N	Y	Y			Included
Potdar, 2023	Y	Y	Y	Y	Y	N	Y	Y			Included
Soundarya, 2022	Y	Y	Y	Y	Y	N	Y	Y			Included
	Score based on appropriate JBI appraisal for case control study										
	1	2	3	4	5	6	7	8	9	10	
Agrawal, 2018	Y	Y	Y	Y	Y	N	N	Y	Y	Y	Included

3. Results

3.1. Study Selection

The comprehensive search strategy across 3 databases (PubMed, Cochrane Library, and ScienceDirect) initially identified 67 records. After removing 3 duplicates, 64 studies were screened by title and abstract. A total of 33 were excluded at this stage, mainly because they focused on populations not relevant to postmenopausal women or investigated conditions outside periodontal disease. Subsequently, 31 articles were reviewed in full, but 26 were excluded, primarily for including inappropriate participant groups (e.g., mixed-gender or younger populations, having a systemic health condition) or using designs that did not allow biomarker analysis in relation to periodontal severity. This rigorous filtering ensured that only studies directly addressing biological markers in postmenopausal women with periodontal disease without any intervention were retained. Ultimately, 5 studies met the eligibility criteria and were synthesized in this study.

3.2. Characteristics of Included Studies

The 5 included studies were conducted between 2015 and 2025, with 4 from India and 1 from Indonesia, reflecting a regional focus where periodontal disease and menopausal health intersect as significant public health issues. Designs varied between cross-sectional (n=4) and case-control (n=1). Sample sizes were modest, ranging from 12 to 49 participants, which limited generalizability but provided focused insights into biomarker behavior. The diversity of biomarkers studied, ranging from bone density measures to salivary cytokines and systemic enzymes, demonstrated the multidimensional approach needed to understand periodontal severity in postmenopausal women.

3.3. Findings of Individual Studies

3.1.1. Pavithra et al., 2024 (India)

This cross-sectional evaluative study uniquely combined skeletal and salivary markers by assessing bone mineral density (BMD) and salivary calcitonin in 12 postmenopausal women with periodontitis compared to controls. BMD was significantly lower in the affected group (0.340 ± 0.089) than in controls (0.375 ± 0.046), showing systemic bone resorption in postmenopause contributes to periodontal vulnerability. Interestingly, salivary calcitonin levels were elevated (1.582 ± 0.578 vs. 1.072 ± 0.349), possibly reflecting a compensatory endocrine response to counteract ongoing bone loss. This duality showed how systemic skeletal health and local oral biomarkers are interconnected, suggesting that monitoring both parameters could offer a more holistic evaluation of disease severity in postmenopausal women.

3.1.2. Hutomo et al., 2021 (Indonesia)

A total of 49 healthy postmenopausal women were investigated for serum alkaline phosphatase (ALP) and serum calcium. ALP levels were strongly associated with periodontal severity, reinforcing its role as a marker of bone turnover. Unlike other studies that relied solely on salivary biomarkers, Hutomo et al. emphasized systemic blood markers, which carry the advantage of being less influenced by local oral conditions. Serum calcium (8.94 ± 0.33) was relatively stable but showed subtle differences between healthy and periodontitis groups, suggesting that while calcium homeostasis was tightly regulated, minor fluctuations reflected local bone demineralization processes. This study emphasized the feasibility of using widely available clinical blood tests to infer periodontal disease risk in postmenopausal women, which could be particularly useful in primary healthcare settings.

3.1.3. Potdar et al., 2023 (India)

Potdar and colleagues analyzed salivary IL-8 and calcium levels in 26 postmenopausal women with periodontitis. Markedly elevated IL-8 levels (983.08 ± 839.82) were reported, confirming the role of pro-inflammatory cytokines in amplifying local periodontal destruction. Interestingly, calcium levels were reduced (6.25 ± 1.647), which indicates compromised mineralization in the oral environment. The strength of this study lies in its emphasis on inflammatory mediators rather than purely structural or hormonal markers, thereby shifting focus toward immune dysregulation as a central factor in postmenopausal periodontal disease. By positioning IL-8 as a sensitive and non-invasive salivary

marker, this study adds practical value, since saliva sampling is patient-friendly and feasible in both studies and routine dental settings.

3.1.4. Soundarya et al., 2022 (India)

A total of 20 women were examined, comparing menstruating controls with postmenopausal participants, and the biomarker focus was on salivary estradiol and calcium. Postmenopausal women showed markedly lower estradiol levels (5.61 ± 5.02), reflecting the well-established hormonal decline during menopause. Salivary calcium was also lower (4.39 ± 2.75), which partly explained reduced mineral support for alveolar bone and periodontal tissue stability. By directly distinguishing menstruating and postmenopausal women, the study elegantly demonstrated how estrogen deficiency sets the stage for periodontal breakdown. Unlike studies focusing on inflammatory markers, this work emphasized hormonal pathways as primary drivers of periodontal vulnerability, suggesting that estradiol deficiency had both systemic and localized oral health consequences.

3.1.5. Agrawal et al., 2018 (India)

As the earliest of the included studies, this case-control study investigated salivary TNF-α in 20 premenopausal and postmenopausal women with periodontitis. TNF-α levels were significantly higher in postmenopausal women (2.05 ± 1.11), showing the chronic pro-inflammatory environment that exacerbated periodontal disease. Unlike biomarkers such as ALP or calcium, TNF-α directly reflected immune system activity, making it an important predictor of disease progression rather than just tissue status. The study added historical depth to the evidence base, confirming that inflammatory cytokines such as TNF-α remain elevated years after the onset of menopause, linking persistent immune activation to long-term periodontal severity.

3.4. Overall Synthesis

The 5 studies underscore that periodontal severity in postmenopausal women arises from a complex interplay of systemic bone metabolism, local inflammatory responses, and hormonal decline. Pavithra and Hutomo emphasized bone-related markers (BMD, ALP, calcium), Potdar and Agrawal showed pro-inflammatory cytokines (IL-8, TNF-α), and Soundarya shed light on the pivotal role of estrogen deficiency. Together, these results showed that no single biomarker was sufficient in isolation; instead, a composite approach integrating skeletal, inflammatory, and hormonal markers may provide a more accurate picture of periodontal severity. The use of saliva as a diagnostic medium in several studies points toward a promising non-invasive strategy for monitoring disease progression in postmenopausal women. However, heterogeneity in design, small sample sizes, and regional clustering of studies limit the generalizability of findings, emphasizing the need for larger, multicenter trials to validate these biomarkers across diverse populations.

4. Discussion

The results of this systematic review showed the growing recognition of biological markers as valuable adjunctive tools in the diagnosis and monitoring of periodontal disease in postmenopausal women. The menopausal transition, marked by a decline in estrogen, fundamentally altered systemic and oral immune responses, creating an environment of increased susceptibility to periodontal tissue breakdown and complicating clinical management.[23] Menopause was also associated with broader changes in the oral microenvironment, such as shifts in salivary composition, alterations in mineral metabolism, and modulation of mucosal immunity, which collectively heightened vulnerability to inflammation and periodontal destruction.[1] In this context, the search for non-invasive, reliable biomarkers was particularly timely, holding potential for improving early detection, refining risk stratification, and enabling more personalized care that takes into account the unique biological context of postmenopausal women. [2]

4.1. Bone-Related Markers

The studies by Pavithra et al. and Hutomo et al. provided compelling evidence that systemic skeletal changes during menopause are closely intertwined with periodontal outcomes. Pavithra et al. demonstrated that postmenopausal women with periodontitis had lower BMD alongside elevated salivary calcitonin, suggesting that systemic bone loss and compensatory hormonal activity both manifest in the periodontal microenvironment.[3,4] While calcitonin can reflect the body's effort to regulate calcium metabolism, its elevation indicates ongoing dysregulation in bone homeostasis that is insufficient to protect alveolar bone from resorption. These results are consistent with previous evidence

showing that estrogen deficiency accelerates bone turnover and increases the risk of periodontal breakdown.[4,5]

Hutomo et al. further corroborated the skeletal link by showing that serum ALP, a key enzyme in bone remodeling, correlates strongly with periodontal severity. ALP elevation reflects heightened bone turnover, reinforcing the concept that alveolar bone loss in postmenopausal women is not merely a local process but part of a systemic skeletal phenomenon.[12,13] Interestingly, while serum calcium levels remained within relatively normal ranges, the subtle differences observed between groups may reflect localized changes in mineralization processes within the alveolar bone. These studies emphasize that bone-related biomarkers provide critical systemic context for understanding periodontal vulnerability in postmenopausal women and may serve as important adjuncts to standard periodontal assessment.

4.2. Inflammatory Cytokines

The role of inflammatory mediators was strongly reinforced by Potdar et al. and Agrawal et al., both of whom demonstrated that pro-inflammatory cytokines are significantly altered in postmenopausal women with periodontitis. Potdar et al. reported markedly elevated salivary IL-8 levels in affected women, emphasizing the role of chemokines in amplifying neutrophil recruitment and sustaining destructive inflammatory cascades in the periodontium.[7,8] IL-8 is particularly valuable as a biomarker because it reflects active inflammation rather than merely structural changes, making it a sensitive indicator of current disease activity.

Agrawal et al. provided further evidence of the inflammatory link by showing elevated salivary TNF-α in postmenopausal women with periodontitis.[3–5] TNF-α plays a significant role in periodontal breakdown by stimulating osteoclast differentiation, enhancing connective tissue degradation, and perpetuating the inflammatory cycle. Its elevation in postmenopausal women is especially relevant, as estrogen deficiency is known to intensify pro-inflammatory cytokine expression. The significance of these results is consistent with the broader literature highlighting TNF-α and IL-1β as central mediators of periodontal destruction and bone resorption.[18,23–26] Importantly, both IL-8 and TNF-α are measurable in saliva, which not only facilitates non-invasive diagnosis but also enables repeated monitoring of disease progression or treatment response in clinical practice.[8] This practical advantage strengthens the case for incorporating cytokine-based assays into everyday periodontal care.

4.3. Hormonal Influence

Hormonal influences were most clearly demonstrated in the study by Soundarya et al., who found significantly lower salivary estradiol and higher salivary calcium levels among postmenopausal women compared with menstruating controls.[9,10] Estradiol plays a major role in maintaining periodontal health by modulating vascular supply, collagen synthesis, and immune balance. Its deficiency can lead to impaired repair mechanisms, heightened inflammatory responses, and increased susceptibility to alveolar bone loss.[11],[14] The observed rise in salivary calcium levels in Soundarya's study suggests altered mineral homeostasis, which further contributes to alveolar bone fragility and periodontal attachment loss.

These results echo a broader study linking reduced estrogen to worsened periodontal outcomes and increased oral dryness, both of which can exacerbate plaque accumulation and tissue damage.[27–29] Importantly, the inclusion of menstruating women as a control group provided a strong contrast, demonstrating that the decline in estradiol, not chronological aging alone, accounts for the worsened periodontal profile in postmenopausal women. Therefore, estradiol may serve not only as a diagnostic marker of menopausal status but also as a predictive indicator of periodontal risk.[30,31] These results emphasized the need for interdisciplinary collaboration between dental and women's health providers, especially in tailoring care for patients undergoing or completing the menopausal transition.

4.4. Integrated Interpretation

When considered collectively, the 5 studies demonstrated that the pathogenesis of periodontitis in postmenopausal women was multifactorial, involving systemic bone metabolism, local inflammatory responses, and hormonal alterations. Bone-related markers such as BMD, ALP, and calcitonin captured the skeletal context of periodontal fragility, while inflammatory mediators such as IL-8 and TNF-α showed active immune dysregulation driving tissue destruction. Hormonal indicators, such as estradiol and calcium, reflect upstream endocrine changes that influence both skeletal integrity and inflammatory

susceptibility. These markers offer a more complete picture of disease mechanisms than any single biomarker alone.

This integrative framework is consistent with the broader literature advocating for multimarker diagnostic models that combine biological and clinical indicators to improve predictive accuracy.[17,31] Such composite approaches can help identify women at particularly high risk, for example, those with low BMD, elevated ALP, increased salivary IL-8, and reduced estradiol levels who can require closer periodontal monitoring and earlier intervention. This direction reflects the ongoing shift toward precision dentistry, where diagnostic and therapeutic strategies are tailored to the unique biological risk profile of each patient.[32]

4.5. Limitations and Future Directions

Despite the promising results, several limitations must be acknowledged. The included studies were predominantly cross-sectional with small sample sizes, limiting their ability to establish causality or capture longitudinal dynamics of biomarker fluctuations. In addition, most studies originated from India and Indonesia, which raised concerns about the generalizability of results to other populations with different genetic, lifestyle, and dietary backgrounds. Methodological heterogeneity was also evident in terms of biomarker assays, periodontal diagnostic criteria, and definitions of menopausal status, complicating comparisons across studies. [5, 21] Potential confounders such as systemic comorbidities, medication use, nutritional factors, and lifestyle behaviors (e.g., tobacco use) were not consistently controlled, even though they independently influenced biomarker levels and periodontal outcomes.

Future studies must prioritize large-scale, multicenter longitudinal studies with standardized biomarker protocols to validate and extend these findings. Technological advances in biosensors, multiplex assays, and point-of-care devices hold significant promise for clinical translation, enabling rapid and cost- effective biomarker assessment in routine dental practice.[27,28] From a public health perspective, the development of non-invasive biomarker panels specifically tailored to postmenopausal women could improve early detection, support personalized preventive care, and strengthen interdisciplinary collaboration between dentistry, gynecology, and endocrinology. Ultimately, such innovations have the potential to reduce the burden of periodontal disease and improve overall health outcomes in this high-risk population.

5. Conclusion

In conclusion, this systematic review consolidates current evidence on biological markers associated with periodontal disease severity in postmenopausal women. The 5 included studies consistently demonstrate that markers of bone metabolism (BMD, serum ALP, salivary calcitonin), inflammatory cytokines (salivary IL-8, TNF-α), and hormonal mediators (salivary estradiol, calcium) provide meaningful insights into the multifactorial nature of periodontal deterioration after menopause. The evidence suggests that estrogen deficiency not only accelerates systemic bone resorption but also amplifies inflammatory pathways and impairs local tissue defense, thereby exacerbating periodontal breakdown.

The review shows that no single biomarker is sufficient in isolation; rather, the integration of skeletal, inflammatory, and hormonal markers may yield the most accurate and clinically useful assessment of periodontal risk. The predominance of non-invasive salivary assays across the studies emphasized their potential feasibility for routine chairside application, offering patient-friendly tools for screening and longitudinal monitoring. At the same time, methodological limitations, including small sample sizes, cross-sectional designs, and regional clustering of studies, underscore the urgent need for larger, multicenter, longitudinal investigations using standardized biomarker protocols.

From a clinical and public health standpoint, validated biomarker panels tailored to postmenopausal women transform periodontal care by enabling early identification of high-risk individuals, guiding targeted preventive interventions, and fostering interdisciplinary collaboration between dentistry and women’s health providers. Ultimately, advancing biomarker-based diagnostics can not only improve oral outcomes but also enhance systemic health in this vulnerable population.

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7. Conflict of Interest

None of the authors have conflicts of interest.

8. Authors' Contributions

Megawati contributed as the main author and was responsible for the conception, literature review, and manuscript preparation, while Pitu Wulandari served as the corresponding author and supervised, reviewed, and approved the final version of the manuscript. Lutfi Putra Perdana was responsible for review and final editing draft.

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