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Periodontal Health and Systemic C-Reactive Protein in Postmenopausal Women: A Review

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Abstract: Periodontal disease is a chronic inflammatory condition that has been increasingly associated with systemic inflammation, as indicated by elevated C-reactive protein (CRP) levels. Postmenopausal women are particularly susceptible due to estrogen deficiency–related alterations in bone metabolism, immune regulation, and inflammatory responses. Available evidence indicates that postmenopausal women exhibit a higher prevalence and greater severity of periodontal disease, often accompanied by increased CRP or high-sensitivity CRP levels, suggesting an enhanced systemic inflammatory burden. Estrogen deficiency contributes to alveolar bone loss and increased production of pro-inflammatory cytokines, while chronic periodontal infection acts as a persistent inflammatory stimulus, together promoting elevated CRP synthesis. Factors such as body mass index, diabetes mellitus, smoking, and hormone replacement therapy may modify this association. Overall, the literature supports a significant relationship between periodontal status and CRP levels in postmenopausal women, underscoring the importance of periodontal health in reducing systemic inflammation and related health risks.

Keywords: *Postmenopausal Women; Periodontal Disease; Periodontitis; C-Reactive Protein; High-Sensitivity C-Reactive Protein; Systemic Inflammation; Estrogen Deficiency; Alveolar Bone Loss; Menopause; Oral-Systemic Health.*

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I. INTRODUCTION

Periodontal disease is a chronic inflammatory disorder affecting the supporting structures of the teeth and is initiated by pathogenic microbial biofilms that elicit a host immune–inflammatory response. Sustained periodontal inflammation results in progressive destruction of periodontal connective tissues and alveolar bone and has been increasingly linked to an elevated systemic inflammatory burden (1,2). Consequently, periodontitis is now recognized not only as a localized oral disease but also as a potential contributor to systemic pathology through the dissemination of inflammatory mediators and the translocation of periodontal pathogens into the systemic circulation (2).

C-reactive protein (CRP) is a well-established acute-phase reactant synthesized predominantly by hepatocytes in response to pro-inflammatory cytokines, particularly interleukin-6. Circulating CRP concentrations serve as a sensitive biomarker of systemic inflammation and are widely used to assess cardiovascular disease, diabetes mellitus, and other chronic inflammatory conditions (3). A growing body of evidence demonstrates significantly elevated CRP levels in individuals with periodontal disease, supporting the hypothesis that periodontal inflammation contributes to systemic inflammatory load (4). Moreover, documented reductions in CRP concentrations following periodontal therapy further substantiate a causal relationship between periodontal health and systemic inflammation (5).

Physiological conditions characterized by altered hormonal and immunological states—such as pregnancy and menopause—are associated with heightened inflammatory responses and increased susceptibility to periodontal disease. Among these, postmenopause represents a critical period marked by estrogen deficiency, which profoundly influences

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bone metabolism, immune regulation, and inflammatory pathways. The decline in estrogen levels following menopause accelerates alveolar bone resorption, exacerbates periodontal tissue breakdown, and promotes the expression of pro-inflammatory cytokines (6). In parallel, menopause-related hormonal alterations have been independently associated with elevated CRP levels, suggesting an increased systemic inflammatory state (7).

The concurrence of estrogen deficiency–related inflammatory changes and chronic periodontal infection may exert a synergistic effect, amplifying systemic inflammation in postmenopausal women. Despite growing evidence linking periodontal disease and CRP levels individually to menopause, the interplay between periodontal status and systemic inflammation in this population remains incompletely elucidated. Therefore, the aim of this review is to critically evaluate the association between periodontal disease and CRP levels in postmenopausal women and to highlight the importance of periodontal health as a potential modifiable factor in reducing systemic inflammation and related health risks in this vulnerable population.

II. PERIODONTAL STATUS IN POSTMENOPAUSAL WOMEN

Estrogen is a principal regulator of bone metabolism in both women and men and plays a critical role in maintaining skeletal homeostasis (8). It exerts direct effects on osteocytes, osteoblasts, and osteoclasts and suppresses osteoclast activation through both direct mechanisms and indirect pathways mediated by osteoblasts and T lymphocytes. Through these coordinated actions, estrogen limits bone turnover and resorption while preserving bone formation (8). Following menopause, estrogen deficiency disrupts this tightly regulated balance, resulting in increased osteoclastic activity and diminished osteoblastic function. Consequently, accelerated alveolar bone resorption occurs, increasing susceptibility to periodontal attachment loss and tooth loss in postmenopausal women (9,10).

Beyond its role in bone remodeling, estrogen deficiency is associated with heightened systemic and local inflammatory responses. Reduced estrogen levels after menopause have been linked to increased expression of pro-inflammatory cytokines, including interleukin (IL)-1, IL-6, IL-8, IL-10, tumor necrosis factor-α, granulocyte colony-stimulating factor, and granulocyte–macrophage colony-stimulating factor (11,12). These inflammatory mediators promote osteoclast differentiation and activity, disrupt bone cell proliferation, and enhance resorption of both skeletal and alveolar bone, thereby contributing to the progression of periodontal disease. The presence of estrogen receptors in gingival tissues and the periodontal ligament further supports a direct hormonal influence on periodontal structures and provides a biological rationale for the periodontal benefits observed with hormone replacement therapy in postmenopausal women (13).

In addition to hormonal and inflammatory alterations, menopause-related vascular changes may further compromise periodontal health. Scardina and Messina reported significant modifications in oral microcirculation among postmenopausal women, including reduced capillary density and impaired blood flow. These changes may limit oxygen and nutrient delivery to periodontal tissues, increasing susceptibility to inflammation and disease progression (14). Complementing these findings, Lee et al. demonstrated that periodontitis progression in postmenopausal states follows a distinct pathogenic mechanism driven by estrogen deficiency–associated immune dysregulation and altered osteogenic balance. This process is characterized by increased inflammatory mediator production, enhanced osteoclast activation, and accelerated alveolar bone loss, ultimately leading to more severe periodontal tissue destruction (15).

A growing body of epidemiological and clinical evidence indicates a higher prevalence and increased severity of periodontal disease in postmenopausal women compared with premenopausal women. Studies have consistently reported greater periodontal attachment loss, increased probing depths, and more pronounced alveolar bone resorption in postmenopausal populations, suggesting heightened susceptibility to periodontitis following menopause (10). Rajan et al. (2020) reported a high prevalence of periodontal disease among postmenopausal women, with gingivitis affecting 71.61% and periodontitis 20.3% of the study population, emphasizing the need for improved preventive oral care strategies in this group (16). Tezal et al. demonstrated a significant association between reduced bone mineral density and periodontitis in postmenopausal women, indicating that systemic bone loss may contribute to periodontal breakdown (10). Similarly, Reinhardt et al. reported that estrogen deficiency and osteoporosis were associated with increased periodontal disease severity in postmenopausal women (17). Furthermore, Sharma et al. observed that periodontal inflammation and disease severity increased with the duration of menopausal years, highlighting the cumulative impact of prolonged estrogen deficiency on periodontal health (18). Riggs further described that estrogen regulates bone resorption primarily by suppressing osteoclast differentiation, activity, and lifespan, and that estrogen deficiency results in increased bone resorption through enhanced osteoclastic function (19).

III. CRP AS A SYSTEMIC MARKER

C-reactive protein (CRP) is a major acute-phase reactant synthesized predominantly by hepatocytes in response to systemic inflammation, primarily under the stimulation of pro-inflammatory cytokines such as interleukin-6 (3). CRP plays a critical role in innate immunity by binding to phosphocholine residues on damaged cell membranes and microbial components, thereby activating the complement cascade and promoting opsonization and phagocytosis. Owing to its rapid and marked increase in circulating concentrations during inflammatory states, CRP is widely utilized as a sensitive biomarker for assessing systemic inflammatory burden (20).

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In clinical practice, CRP levels are measured using either conventional CRP assays or high-sensitivity CRP (hs-CRP) assays. Conventional CRP assays detect relatively high CRP concentrations and are primarily employed to identify acute infections or overt inflammatory conditions. In contrast, hs-CRP assays are capable of detecting much lower CRP concentrations and are particularly useful for identifying chronic low-grade inflammation, even in apparently healthy individuals (20). Elevated hs-CRP levels have been consistently associated with an increased risk of cardiovascular disease, metabolic syndrome, and other chronic inflammatory disorders, underscoring the clinical relevance of low-grade systemic inflammation in disease pathogenesis (21).

IV. CRP IN PERIODONTITIS

Periodontitis is a chronic inflammatory disease that is increasingly recognized as a significant contributor to systemic inflammatory status. Loos reported that individuals with periodontal disease consistently exhibit elevated circulating levels of systemic inflammatory mediators, including C-reactive protein (CRP), reflecting a sustained low-grade inflammatory response rather than an acute inflammatory state (22). The elevation of CRP in periodontitis has been attributed to the systemic dissemination of periodontal pathogens and the release of pro-inflammatory cytokines from inflamed periodontal tissues into the circulation (22).

Clinical and epidemiological studies provide strong support for this association. Salberz et al. demonstrated a significant relationship between aggressive periodontitis and elevated serum CRP levels, with generalized aggressive periodontitis exhibiting significantly higher CRP concentrations than localized aggressive periodontitis and periodontally healthy controls. These findings suggest a greater systemic inflammatory burden associated with more extensive periodontal involvement (23). Moreover, even localized periodontal infections characterized by chronic inflammation and progressive tissue destruction have been shown to elicit systemic host responses, as evidenced by increased circulating levels of acute-phase reactants such as CRP (25).

A range of inflammatory mediators, including CRP, interleukin-6, and neutrophils, are elevated in the peripheral blood of individuals with periodontal disease, indicating that periodontal inflammation may either directly contribute to their systemic elevation or signal distant organs—particularly the liver—to upregulate their production (26). The translocation of periodontal bacteria, bacterial products such as lipopolysaccharides, and locally produced cytokines into the bloodstream reinforces the role of periodontitis as a chronic source of systemic inflammation (28). Consequently, elevated CRP levels in individuals with periodontal disease reflect the contribution of periodontal infection to the overall low-grade inflammatory burden (27).

The magnitude of systemic inflammation appears to be closely related to the extent and severity of periodontal involvement. Higher CRP concentrations have consistently been observed in individuals with generalized periodontitis compared with those with localized disease, suggesting that the total volume of inflamed periodontal tissue plays a critical role in determining systemic inflammatory response (29). Increased severity of periodontal inflammation is also associated with greater frequency and magnitude of bacteremia, further stimulating hepatocyte CRP synthesis and interleukin-6 release by circulating leukocytes (29). Dentate individuals with extensive periodontal disease have been reported to exhibit approximately one-third higher mean CRP levels and a twofold higher prevalence of elevated CRP compared with periodontally healthy individuals (30).

Two complementary mechanisms may explain the association between periodontal disease and elevated CRP levels. First, a shared hyperinflammatory phenotype may predispose certain individuals to both periodontal disease and heightened systemic inflammation. Second, a synergistic pathway may exist whereby periodontal infection amplifies systemic CRP levels, particularly in the presence of other modifying risk factors such as metabolic disorders and hormonal changes (27,30). Notably, CRP levels have been shown to increase during the menopausal transition independent of aging and adiposity, suggesting that estrogen decline may further enhance systemic inflammatory responses and potentially exacerbate periodontal inflammation in postmenopausal women (24).

V. PERIODONTAL STATUS AND CRP IN POST MENOPAUSAL WOMEN

Several investigations conducted specifically among postmenopausal women have demonstrated a significant association between periodontal disease severity and elevated systemic inflammatory markers, particularly C-reactive protein (CRP). Compared with premenopausal women, postmenopausal women more frequently exhibit deeper periodontal pockets, greater clinical attachment loss, and increased alveolar bone resorption, reflecting a higher overall burden of periodontal disease following menopause (31,32). These periodontal changes are largely attributed to menopause-related hormonal alterations, particularly estrogen deficiency, which adversely affect periodontal tissue turnover, bone metabolism, and host immune responses.

In parallel with deteriorated periodontal status, postmenopausal women with periodontitis commonly present with elevated serum CRP and high-sensitivity CRP (hs-CRP) levels. Esteves-Lima et al. reported that individuals with more extensive and severe periodontal inflammation exhibited significantly higher CRP concentrations, even after adjustment for major confounding variables, including age and metabolic factors (33). These findings support a direct relationship between the extent of periodontal inflammation and the magnitude of systemic inflammatory burden in postmenopausal women.

The observed association between periodontitis and CRP elevation in this population is thought to be mediated by a synergistic interaction between estrogen deficiency and

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chronic periodontal inflammation. Reduced estrogen levels after menopause promote osteoclastic bone resorption, impair immune regulation, and enhance the production of pro-inflammatory cytokines—particularly interleukin-6, a key mediator of hepatic CRP synthesis (15,34). When this hormonal imbalance coexists with persistent periodontal infection, the cumulative inflammatory stimuli may result in greater systemic CRP elevation than that induced by either condition alone (15,29).

Interpretation of these associations must consider the influence of potential confounding and modifying factors. Increased body mass index and adiposity are independently associated with elevated CRP levels and may amplify inflammatory responses in postmenopausal women (35). Metabolic conditions such as diabetes mellitus further exacerbate periodontal destruction and systemic inflammation, whereas hormone replacement therapy has been reported in some studies to improve periodontal parameters and reduce inflammatory marker levels (32,36). Studies that appropriately adjust for these variables provide the most robust evidence supporting an independent association between periodontal disease severity and elevated CRP concentrations in postmenopausal women.

Table 1 summarizes key studies evaluating the relationship between periodontal disease, menopause, and systemic inflammatory markers, with particular emphasis on C-reactive protein, underscoring the multifactorial nature of systemic inflammation in postmenopausal women.

Table 1. Studies Assessing the Association Between Periodontitis and C-Reactive Protein During the Menopausal Transition

Author (Year)	Study Design	Population	Variables Assesed	Key Findings
El Khoudary et al. (2025)	Longitudinal cohort (SWAN study)	Peri- and postmenopausal women	Menopause transition, CRP	CRP increases during menopausal transition independent of age/adiposity
Esteves-Lima et al. (2023)	Cross-sectional	Adults incl. postmenopause	Periodontitis, CRP	Higher CRP in severe periodontitis
Rajan et al. (2020)	Retrospective cross-sectional	Postmenopausal women	Periodontal status	High prevalence of gingivitis (71.6%) and periodontitis (20.3%) in postmenopausal women
Sharma et al. (2018)	Cross-sectional	Postmenopausal women	CRP, periodontitis	CRP rises with menopausal years
Lee et al. (2018)	Experimental/Observational	Postmenopausal state models	Estrogen deficiency, inflammatory mediators, alveolar bone	Estrogen deficiency altered immune regulation and accelerated periodontitis progression
Scardina & Messina (2012)	Observational	Postmenopausal women	Microcirculation, periodontitis	Altered oral microcirculation
Salberz et al. (2006)	Case-control	Periodontitis patients	Aggressive periodontitis, CRP	Generalized periodontitis showed significantly higher CRP
D'Aiuto et al. (2006)	Interventional	Periodontitis patients	Periodontal therapy, CRP	CRP reduced after periodontal treatment
López-Marcos et al. (2005)	Clinical study	Postmenopausal women on HRT	Periodontal parameters, HRT	HRT is associated with improved periodontal parameters
Amar & Han (2003)	Review	General population	Periodontal infection & systemic disease	Periodontal infection contributes to systemic inflammation
Loos et al. (2000)	Cross-sectional	Periodontitis patients	Systemic inflammatory markers	Periodontitis patients had elevated CRP and IL-6
Tezal et al. (2000)	Cross-sectional	Postmenopausal women	BMD, periodontitis	Low BMD associated with periodontitis
Visser et al. (1999)	Population study	Adults	BMI, CRP	Obesity is associated with elevated CRP
Reinhardt et al. (1999)	Cross-sectional	Postmenopausal women	Periodontal status, BMD	Estrogen deficiency linked with severe periodontitis

VI. CONCLUSION

The association between periodontal disease and elevated C-reactive protein levels in postmenopausal women

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has important clinical implications. Estrogen deficiency and periodontal inflammation may act synergistically to increase systemic inflammatory burden, potentially contributing to broader health risks in this population. These findings highlight the need for routine periodontal assessment and early intervention in postmenopausal women, particularly those with additional risk factors such as obesity or diabetes. Incorporating periodontal care into comprehensive health management may aid in reducing systemic inflammation and improving overall health outcomes in postmenopausal women.

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