



## Review Article

# Could treating periodontitis prevent osteoporosis? An update of the last decade

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**Abstract**

Chronic periodontitis and osteoporosis are both systemic diseases, characterized by bone resorption. Over the last decade, their correlation has been examined closely, mainly to investigate whether they present a risk factor or an indicator for each other. It is their pathogenetic similarities, their numerous common risk factors and their frequent concomitant development that initiated researchers' interest in the precise association between these two maladies. The present review is aiming to analyse this correlation, laying emphasis on the effects of periodontal status on the skeletal bone mineral density, as suggested by the latest studies. It will also attempt to clarify whether periodontal management could influence the progression or the onset of osteoporosis.

**Keywords:** Chronic periodontitis, Osteoporosis, Risk factors, Bone mineral density

## Common pathogenetic patterns and differences between osteoporosis and periodontitis

Chronic periodontitis is considered to be an inflammatory condition caused by microorganisms that colonize teeth surface below the gingival margin<sup>1</sup>. This periodontal infection leads to alveolar bone loss and eventually tooth loss, if left untreated<sup>2</sup>. On the other hand, osteoporosis is also defined by bone mass density degradation along with bone microstructural distortion and high fracture risk. However, the latter numbers among bone metabolic diseases, without implicating any microbial infection<sup>3</sup>. Despite the lack of microbiological parameter in osteoporosis, both diseases are indisputably linked by their chronic profile and the bone resorption they cause. Moreover, there have been suggestions that low bone density in the oral cavity might be an individual factor, which influences the escalation of periodontitis, as well as, the inflammatory response to the periodontal infection<sup>4,5</sup>. The correlation between these two diseases expands to a large number of risk factors that they share, such as age, hormonal status, smoking, serum levels of calcium and vitamin D and genetic susceptibility. In fact, chronic periodontitis and osteoporosis can also be considered as risk factors for each other, presenting common impacts and, thus, requiring a combined simultaneous treatment<sup>6</sup>. This aspect is firmly

noticed among postmenopausal women, who frequently suffer from both osteolytic conditions<sup>7</sup>. Rank-ligand, which plays a dominant role in postmenopausal osteoclastogenesis augmentation, is found overexpressed in human oral epithelial cells after infection with *Porphyromonas gingivalis*, a bacteria responsible for the majority of periodontal maladies<sup>8</sup>. In addition, a recent cross-sectional study classified 94 postmenopausal women according to their periodontal status and t-scores, confirming that the severity of periodontitis is correlated statistically with osteoporosis<sup>9</sup>.

## Common risk factors and comorbidities

Periodontitis has often been reported as a systematic disease independently associated with a range of

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comorbidities, including type 2 diabetes, rheumatoid arthritis, psoriasis, respiratory infections and osteoporosis. Besides the apparent bone loss that both diseases have as a common place, there is a significant number of common risk factors, the most important of which are presented below<sup>10</sup>.

**1) Age:** It has been proven by numerous studies, that the risk of low energy fractures increases significantly by age in both sexes. These types of fractures occur due to low bone mineral density and disturbed microarchitecture, both of which characterize osteoporosis. Hence, this metabolic bone disease is inevitably linked with aging. To be more specific, the prevalence of osteoporosis is currently increasing worldwide probably due to the expansion of the elderly population, along with the prolongation of life expectancy<sup>11-14</sup>. The underlying mechanism of the precedent correlation includes sex hormones and blood nutrients deficiency, as well as, the accumulation of Reactive Oxygen Species (ROS)<sup>3</sup>.

The incidence of chronic periodontitis also increases with age. There is in fact a significant association between age and the severity of periodontal disease. The deterioration of the immune system and the insufficiency of certain blood nutrients, such as cis- $\beta$ -carotene folate and vitamin D, which are frequently observed in elderly, might be involved in the relationship between aging and periodontal disease<sup>15,16</sup>.

**2) Smoking:** Smoking has been firmly associated independently with osteoporosis by a plethora of studies<sup>16,17</sup>. Baccaro LF. et al. found that regular smoking (a pack of cigarettes per day or more) presently or in the past promotes an early onset of the disease among postmenopausal women<sup>18</sup>. An other study warns both active and former smokers about the deleterious effects of this habit on trabecular bone mass, irrespective of Chronic Obstructive Pulmonary Disease (COPD)<sup>19</sup>, while elderly male smokers are not deprived of smoking's catastrophic impact on bone mineral density at both lumbar spine and femoral neck region, as measured by dual energy X-ray absorptiometry (DXA)<sup>20</sup>. Very recently, it has been proven by pQCT and heel ultrasound measurements that even passive smoking in childhood takes its toll on bone mineral density and low energy fractures risk in adulthood<sup>21</sup>.

As far as periodontitis is concerned, scientists have been unanimous in its' correlation with smoking. Clinical evidence underlines the susceptibility of active smokers in developing severe chronic periodontitis and presenting a more aggressive progression of the disease, comparing to non smokers<sup>22</sup>. In addition, tobacco smoking causes statistically significant greater alveolar bone resorption, more extensive probing attachment loss and more frequently tooth loss than non smoking, irrespective of oral hygiene level<sup>23</sup>. Smokers also respond less favorably than non smokers to periodontal treatment<sup>22</sup>. However, participating in cessation programs, not only will ameliorate their response to therapy, but will also reverse many tobacco effects on periodontal tissues<sup>24</sup>.

**3) Vitamin D and Calcium deficiency:** Serum levels of vitamin D and calcium are enlisted to osteoporosis

biomarkers for decades and modern studies continue to confirm their predominant role in the prevention and monitoring of the disease<sup>25,26</sup>. Vitamin D and Calcium supplements are considered to be a golden standard in the management of osteoporosis, as they statistically reduce the risk of low energy fractures, implying that their deficiency is essentially involved in the pathogenesis of this bone metabolic syndrome<sup>27</sup>. Vitamin D deficiency (serum 25(OH) vitD<20 ng/ml) is significantly associated with diminished bone mineral density and osteoporotic fractures<sup>28</sup>, while people, especially the elderly, are often presented with low dietary calcium intake, enhancing the release of this mineral from bones through resorption<sup>29,30</sup>.

Through its' crucial position in bone metabolism and anti-inflammatory activity, vitamin D affects periodontal status as well. The maintenance of serum 25(OH)vitD levels within normal range modulates a patient's respond to periodontal treatment<sup>16,31</sup>. Although vitamin D supplementation is associated with decreasing severity of chronic periodontitis, further investigation is required to establish the vitamin's deficiency as an indisputable risk factor<sup>32</sup>. Insufficient calcium intake has been correlated with periodontal disease mainly through its impact on bone metabolism<sup>33</sup>. It has been suggested, that calcium supplements could improve the severity of chronic periodontitis, but a specific and direct association is yet to be found<sup>34</sup>.

**4) Estrogen levels:** Nowadays, menopause is considered to be the main risk factor for osteoporosis in women. This phenomenon occurs because of the estrogen deficiency that normally takes place. The reduction of estrogen levels increases interleukin-1 (IL-1) and tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ). These cytokines induce bone resorption which, in turn reduces the excretion of parathyroid hormone (PTH). As a consequence, 1,25(OH)<sub>2</sub>D<sub>3</sub> production diminishes and compromises calcium intestinal absorption, a condition that aggravates bone resorption<sup>3,6</sup>.

Estrogen receptors can be spotted on cells of the periodontal ligament, suggesting that estrogen levels interact with periodontal tissues directly. Although postmenopausal women are more likely to develop chronic periodontitis than premenopausal women, further studies are necessary to verify whether this tendency depends exclusively on the impact of estrogen deficiency or is affected by aging<sup>35,36</sup>.

**5) Genetics:** Both periodontitis and osteoporosis are considered to be complex conditions with multifactorial etiology. Inheritance and genetic polymorphisms play their unique role among the other risk factors that these two diseases share<sup>37,38</sup>. Recently, Williams G. and Bassett D. identified 518 genetic locations connected to bone mineral density using genome-wide association analysis on data derived from over 426000 British individuals<sup>37</sup>. The same research revealed protein-coding genes, correlated to the risk of developing osteoporosis, most important of which was DAAM2.

Many studies have also investigated single nucleotide

polymorphisms in periodontitis demonstrating the role of genes linked to the immune system, such as those which code interleukin-1 (IL1), IL 6, IL10 and vitamin D receptor<sup>38</sup>.

**6) Oxidative stress:** The accumulation of reactive oxygen species (ROS) in the cells, which are by-products of oxygen metabolism, causes a stressful imbalance called oxidative stress. Aging is not the only reason behind this condition, as numerous environmental factors, such as UV and ionizing radiation, heavy metals' pollution etc., increase ROS production, outweighing the antioxidant defense of the organism<sup>39</sup>. Researches have proved that ROS affect negatively the Wnt/ $\beta$ -catenin pathway, reducing osteoblastogenesis and subsequently promoting bone resorption and reducing bone mass<sup>3,40</sup>.

According to recent studies, oxidative stress is firmly associated with periodontal disease. Their bond relies on peripheral blood neutrophils, which appear hyperactive in case of periodontitis and are also the main source of ROS<sup>41</sup>. Moreover, ROS, especially  $H_2O_2$ , induce the apoptosis of periodontal ligament cells, via mitochondrial abnormalities, a fact which defines oxidative stress as an independent risk factor for periodontitis<sup>42</sup>.

## A bidirectional association between osteoporosis and chronic periodontal disease

**Osteoporosis as a risk factor for periodontitis:** During the past decade, it has been suggested by many authors that chronic periodontitis could be the localized version of a systemic bone disease such as osteoporosis<sup>43</sup>. Ayed S.M. et al. have conducted a case-control study, demonstrating that osteoporotic postmenopausal women present statistically significant more severe periodontal disease than the non-osteoporotic group. In detail, both groups were subjected to thorough clinical and radiographical examination (including clinical periodontal measurements, DXA and dental radiographs) and root surface of the extracted teeth was analyzed for the elements Ca (calcium), P (phosphorus), F (fluoride), Mg (magnesium) and K (potassium). Osteoporotic group was found with statistically significant greater clinical attachment loss, larger distance between cemento-enamel junction (CEJ) and alveolar crest and lower alveolar bone density. Ca was also detected statistically significantly lower in osteoporotic women<sup>44</sup>. Clinical attachment loss (CAL) equals to the distance between CEJ and the deepest point of a periodontal pocket, and by consequence, presents a very reliable indicator of the alveolar bone loss and the progression of periodontitis. Taking that into consideration, finding CAL statistically significant greater in postmenopausal women with lower bone mineral density (BMD) than in those with normal BMD, underlines the predominant impact of osteoporosis and/or osteopenia on the development of chronic periodontitis<sup>45</sup>. Other researches have exhibited statistical significance in additional periodontal indices, concerning the inflammatory response of gingiva. Richa et al. discovered that osteoporotic postmenopausal women suffer

from more extensive gingival bleeding and dental plaque accumulation than those with normal BMD<sup>46</sup>. An other interesting parameter is the direct correlation between the severity of osteoporosis (usually measured through BMD) and the severity of chronic periodontitis. This is to say that lower BMD results in more severe periodontal disease (higher CAL and alveolar bone loss)<sup>47</sup>. A 3-year cross-sectional Korean study revealed a strong association between BMD and the number of remaining teeth in postmenopausal women, supporting the relationship between osteoporosis and tooth loss, which is the ultimate result of untreated severe periodontitis<sup>48</sup>. Similarly, Jank KM et al., using data from Korea National Health and Nutrition Examination Survey (KNHANES), demonstrated that normal BMD people had significantly larger number of remaining teeth than those who were diagnosed with osteoporosis or osteopenia, irrespective of their gender<sup>49</sup>.

**Periodontitis as a risk factor for osteoporosis:** A 10-year cohort study recently revealed that periodontitis can be considered as an independent risk factor for osteoporosis. This revolutionary project compiled various data from 13464 participants, who were divided into two groups, a test group consisting of periodontal patients who received the whole range of periodontal treatment and a control group matched for sex, age, income, disabilities etc. The results confirmed that periodontal patients are more likely to develop osteoporosis, with females older than 50 years old presenting an even higher risk<sup>50</sup>. Moreover postmenopausal women diagnosed with chronic periodontitis exhibited reduced cortical bone in mandibula, as examined through digital panoramic radiographs, a finding that supports their tendency to develop osteoporosis<sup>51</sup>. An other valuable population-based cohort study monitored 29463 newly diagnosed periodontal patients in comparison with 58926 individuals without periodontal disease for a 6-year period. Eventually patients with slight, moderate and severe periodontitis had 1.56, 2.09 and 2.08 times the risk of osteoporosis respectively, comparing to the group without periodontitis. This outcome associates strongly the severity of chronic periodontitis with the susceptibility to osteoporosis<sup>52</sup>. Lee JH. et al. also conducted a wide research, in which periodontal patients exhibited statistically significant higher risk of osteoporosis than those who maintained a healthy periodontal status<sup>53</sup>.

## The impact of periodontal management on preventing osteoporosis

As elaborated above, periodontal disease could affect independently the progression of osteoporosis. Therefore, scientists reasonably aimed at clarifying the possible impact of periodontal treatment on the onset and development of osteoporosis. A modern study by Baldodia A. et al. revealed promising results on this issue. The researchers recruited 68 postmenopausal women diagnosed with osteopenia and chronic periodontitis. Half of them received scaling and root planning (which is the standard protocol for periodontal

treatment) along with calcium and vitamin D supplements (test group), while the other half (control group) received the exact same supplementation, but without any periodontal therapy. After 6 months, the test group was 4,82 times more likely to obtain a normal BMD than the control group, claiming that a basic periodontal therapy could improve significantly bone mineral density<sup>54</sup>. Another recent study indicates that patients, whose oral hygiene does not comply with their periodontal status (meaning that a sudden periodontal breakdown can occur regardless of their good oral hygiene), should be considered more susceptible to osteoporosis. According to the same research, the maintenance of periodontal health, through controlling oral hygiene, could play an essential role in preventing the development of osteoporosis<sup>55</sup>. Other studies present chronic periodontitis, as a strong indicator of underlying osteoporosis, which has not been diagnosed, obligating dentists to alarm their patients when needed. Dental x-rays, such as panoramic radiographs, provide sufficient information about the thickness of mandibular cortical bone and alveolar trabecular architecture, both of which have been firmly correlated to skeletal bone mineral density. This fact raises the question of whether dental images could be exploited as a low-cost and effortless diagnostic tool for osteoporosis<sup>51,56</sup>. Finally, chronic periodontitis is considered to be a systemic inflammatory disease, and as such, if left untreated, it could contribute to the progression of osteoporosis via cytokine pathways<sup>56</sup>.

## Discussion

Coming to a conclusion, although countless studies have given prominence to the impact of osteoporosis on periodontal disease, only few have investigated the reverse of the coin. Given the prevalence of osteoporosis, as well as, its essential effect on patients' life quality, the unveiling of an early indicator of the disease is more than mandatory. As presented by this review, chronic periodontitis could play that role. It has also been suggested that periodontal management could delay the progression of osteoporosis, giving hope that a simple dental treatment might be able to affect positively such a complicated and challenging bone syndrome. Literature has indicated postmenopausal women as the population most in danger of osteoporosis, hence, it is them who should pay additional attention to their periodontal examination. Disturbingly, the majority of periodontal patients seem to be unaware of their disease, because they correlate oral illness exclusively to the onset of symptoms<sup>57</sup>. This fact points out a necessity to educate people, especially postmenopausal women, on their periodontal management and inform them about the potential benefits that oral health could have on their skeletal well-being. Nevertheless, more research is required to elucidate the impact of chronic periodontitis on osteoporosis, as well as, the exact mechanism by which periodontal therapy ameliorates bone mineral density.

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