

Effect of Osteoporosis on Oral Health

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Abstract

Osteoporosis, a generalized skeletal disease, has emerged as a major health problem affecting middle aged and older individuals. Osteoporosis is a grave social and economic problem for which the dentist has the opportunity to make unique contributions by early identification of patients with the potential for osteoporosis. The disease is associated with several risk factors, and increasing evidence suggests that it may be associated with oral health conditions such as periodontal disease, reduced jaw bone density, tooth loss, inability to create functional dentures and temporomandibular disorders. Women with osteoporosis are three times more likely to experience tooth loss than those who do not have the disease. Systemic loss of bone density in osteoporosis including that of the oral cavity may provide a host system that is increasingly susceptible to infectious destruction of periodontal tissue. Besides the effect of osteoporosis on oral health, bisphosphonate (BP) related osteonecrosis of jaws is a major concern to the dentist. The mandible is more commonly affected than the maxilla (2:1 ratio). Dental treatment seems to be a precipitating event in the development of most cases of BP related osteochemonecrosis. It is therefore imperative that osteoporosis patients for whom BP therapy is being contemplated should have their dental status assessed prior to initiation of the BP therapy. This current review discusses the effect of osteoporosis on oral health, oral implications of osteoporosis therapy as well as bisphosphonates related osteonecrosis of the jaw.

Keywords: Osteoporosis, Oral health, Tooth loss, Periodontal disease, Bisphosphonates related osteonecrosis of jaws

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Introduction

Osteoporosis, a generalized skeletal disease, is a major public health concern that is characterized by low bone mass with micro architectural deterioration of bone tissue leading to enhanced bone fragility [1]. Osteoporosis as described by WHO is a 'progressive systemic skeletal disease characterised by low bone mass and micro architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture' [2]. Osteoporosis has also been operationally defined on the basis of bone mineral density (BMD) [1] assessment. According to the WHO criteria, osteoporosis is defined as a BMD that lies 2.5 standard deviations or more below the average value for young healthy women. This criterion has been widely accepted and provides both a diagnostic and intervention threshold [3].

Osteoporosis is a silent disease, reflected only in a low bone density, till a fracture occurs [1]. Common sites of fracture include the spine, hip, forearm and proximal humerus. Fractures at the

hip incur the greatest morbidity and mortality [3]. Osteoporosis affects more than 200 million persons around the world [4]. More than one-third of adult women aged 60-70 years and two-thirds of women aged 80 years and above have osteoporosis [5]. One in five men sustains one or more osteoporotic fractures in their lifetime [6]. The prevalence of osteoporosis is increasing with increasing age [7]. Osteoporosis is a serious threat in India as well [8]. India is a home to a very large population of osteoporosis patients [9]. Health-care statistics reveal that patients with this disease are often undertreated or incorrectly treated [10]. The burden of morbidity from osteoporosis has significant medical, social and financial implications [11].

Osteoporosis was once considered a physiological process associated with ageing in women, much the same way as tooth loss was thought to be related to age rather than chronic periodontal infection, but today it is recognized as a multifactorial chronic systemic disease. Osteoporosis may also affect the jawbones

resulting in bone loss [12]. Several studies have been conducted over the last few decades to determine the relationship between osteoporosis and oral health. Majority of investigations have studied the association between osteoporosis and periodontal disease, tooth loss and jawbone density [13-18]. According to the current concept, osteoporosis due to the estrogen deficiency represents a variety of conditions in relation to the stability of the structure of the jawbones. Given the evidence that alveolar processes provide the bony framework for teeth support, the loss of systemic bone density in osteoporosis, including that of the oral cavity, can be a negative consequence on tooth stability. It has also been found that the decline of skeletal mass can be correlated with an increased risk of oral bone loss, resulting in a host system that is increasingly susceptible to infectious destruction of periodontal tissues. In spite of these findings, osteoporosis may cause alteration in the mineral content of the alveolar bone and thus can predispose to the progression of periodontal disease [19]. The purpose of this article is to review and summarize published literature concerning possible associations between osteoporosis and various oral conditions such as tooth loss, periodontal disease, dental prosthesis, temporomandibular disorders, oral implications of osteoporosis therapy and bisphosphonates related osteonecrosis of the jaw.

Osteoporosis and Tooth Loss

Teeth are fundamental to quality of life throughout human life [20,21]. An association between tooth loss and osteoporosis has been reported in the literature [22-28]. Women with osteoporosis are three times more likely to experience tooth loss than those who do not have the disease. Among postmenopausal women on hormone replacement therapy, the risk of tooth loss was relatively less. Increased alveolar ridge resorption and greater alveolar crestal height loss was reported in subjects with osteoporosis and osteopenia [18,29,30].

Osteoporosis and Periodontal Disease

Both osteoporosis and periodontal diseases are bone resorptive diseases. Osteoporosis is characterized by reductions in bone mass and may lead to skeletal fragility and fracture. Periodontitis is characterized by resorption of the alveolar bone and is a major cause of tooth loss in adults. Because loss of alveolar bone is a prominent feature of periodontal disease, severe osteoporosis could be suspected of being an aggravating factor in the case of periodontal destruction. Therefore, it has been hypothesized that the breakdown of periodontal tissue may, in part, be related to systemic diseases, including osteoporosis. In addition, literature has proposed the role of osteoporosis in the onset and progression of periodontitis and tooth loss. Bando et al. reported that lower spinal BMD was positively correlated with tooth loss [31]. In a study to determine the risk factors for tooth loss in elderly people, Xie and Ainamo found that tooth loss was associated with a history of bone fracture that was used as an indicator of osteoporosis [32]. Recent literature suggests a possible association between osteoporosis and periodontal disease among postmenopausal females and showed a positive association between the two diseases [33]. Payne et al. in their 2-year longitudinal study evaluated the effect of osteoporosis and cigarette smoking on

alveolar bone height in postmenopausal females [34]. They reported that both smoking and osteoporosis had a negative impact on alveolar bone height. Jabbar et al. evaluated the relationship between periodontal disease and plasma cytokines, vitamin D and BMD in postmenopausal women with and without osteoporosis [35]. They reported that periodontal disease was more common in women with osteoporosis and is associated with lower vitamin D and higher concentrations of receptor activated nuclear factor kappa B ligand and suggested that raised cytokines may play an important role in the association between these two conditions. Mohammad et al in their cross-sectional study on postmenopausal women compared various periodontal parameters in individuals with high and low bone and spine density [18]. They reported that parameters such as gingival recession and clinical attachment level were significantly different in both the groups. The studies showing a positive and negative association between osteoporosis and periodontal disease are shown in **Tables 1 and 2**.

In a comparison of the risk factors associated with osteoporosis and periodontal diseases, it seems clear that there are multiple similarities between the two disease processes. The diseases are associated in general with advancing age, with the vast majority of patients being over the age of 35, and a higher incidence in the later decades. A patient with a history of loss of alveolar bone support is at risk for future progression of periodontitis. Likewise, a patient with systemic bone loss or osteoporosis is at risk for periodontitis. Some of the common risk factors shared by both osteoporosis and periodontal disease are shown in **Table 3**.

Potential mechanism of association

Several potential mechanisms which osteoporosis or systemic bone loss may be associated with periodontal attachment loss, loss of alveolar bone height and tooth loss have been proposed [52]:

Low bone density in the oral bone associated with low systemic bone

Osteoporosis results in loss of BMD throughout the body, including the maxilla and the mandible. The resulting low density in the jawbones leads to increased alveolar porosity, microarchitectural deterioration of trabeculae, reduced remodeling rate, reduction in volume of the residual ridge, and decrease in the cortical thickness following invasion by periodontal pathogens.

Modification of local tissue response to periodontal infections due to systemic factors affecting the bone remodelling

Persons with systemic bone loss are known to have increased systemic production of cytokines (IL 1 and 6) that may have effect on the bone throughout the body including bone of oral cavity. Periodontal infections have been shown to increase local cytokine production that in turn increases local osteoclasts activity resulting in increased bone resorption.

Estrogen-deficiency

Enhances the rate of breakdown of connective tissue components of the gingiva by stimulating synthesis of matrix metalloproteinases (MMP-8, and MMP- 13) [53], nitric oxide

Table 1 Studies showing a positive association between osteoporosis and periodontal disease.

Author	Population	Study Design	Risk Estimate	Result
Kribbs et al. [36]	85 osteoporotic women and 27 normal women	Cross-sectional	OR: 2.7 [95% CI: 1.1-6.5]	Osteoporotic group had less mandibular bone mass and density
Jacobs et al. [37]	69 women receiving hormone replacement therapy aged 32-64 at entry	Prospective longitudinal study	No OR calculated	Positive correlation between spinal density and mandibular bone mass at the second examination (average follow-up 5.1 years)
Streckfus et al. [38]	28 healthy women aged 23 women with periodontitis	Cross-sectional	OR: 2.74 [95% CI: 1.23-6.12]	More alveolar bone loss, more missing teeth, in postmenopausal women with estrogen deficiency
Southard et al. [39]	61 dentate Caucasian women aged 20 to 78 years	Cross-sectional	OR: 5.3 [95% CI: 2.5-11.3]	Significant correlation between the density of maxillary and mandibular alveolar process, lumbar spine, hip and radius
Jeffcoat et al. [40]	158 postmenopausal women	Cross-sectional	OR :5.23	Significant correlation between hip BMD and mandibular basal BMD
von Wowern et al. [41]	112 women with osteoporotic fractures	Cross-sectional	R: 2.7 [95% CI: 1.1-6.5]	Greater amounts of loss of attachment in osteoporotic women with a mean age of 68
Tezal et al. [29]	70 postmenopausal Caucasian women aged 51-78	Cross-sectional	OR :2.89	Mean alveolar bone loss was significantly correlated with systemic BMD
Payne [42]	41 with normal BMD, 17 osteoporotic women	2 - y e a r prospective longitudinal clinical study	OR: 1.73 [95% CI: 1.23-2.43]	Greater alveolar bone loss, crestal and subcrestal density loss in the osteoporotic and estrogen deficient women.
Reinhardt et al. [43]	Women within 5 years of menopause, 59 with adult periodontitis and 16 non-periodontitis. Stratified by serum estradiol level	2 year prospective longitudinal study	OR: 1.68	In non-smoking osteopenic/osteoporotic periodontitis patients with estrogen deficiency had more bleeding on probing and clinical attachment loss
Taguchi et al. [44]	64 women between the ages of 50 and 70 years	Cross-sectional	OR: 2.10	Mean alveolar bone level significantly correlated with systemic BMD
Grodstein et al. [45]	42,171 post-menopausal women	Cross-sectional	OR: 1.35 [95% CI: 1.14-1.59]	Significant correlation between systemic BMD and mandibular basal BMD

Table 2 Studies showing a negative association between osteoporosis and periodontal disease.

Author	Population	Study Design	Risk Estimate	Result
Von Wowern et al. [46]	52 women with osteo-porotic fractures	Cross-sectional	OR: 1.00 [95% CI: 0.98-1.02]	Osteoporotic subjects had not less bone mineral content in their jaw bones
Shrout et al. [47]	65 postmenopausal women with no or mild periodontitis	Cross-sectiona	OR: 1.16 [95% CI: 0.90-1.49]	Complexity of the trabecu-lar pattern weakly correlated with lumbar spine and femoral BMD
Elders et al. [48]	216 females between 46 and 55 years	Cross-sectional	OR: 1.46 [95% CI: 0.97-2.21]	No significant correlation was observed between probing depth, bleeding on probing, missing teeth, alveolar bone height and bone mass
Hildebolt et al. [49]	135 postmenopausal women aged 41-70 years, no moderate, severe periodontitis	Cross-sectional	OR: 1.4 [95% CI: 0.6-3.1]	Attachment loss was corre-lated with tooth loss but not with BMD
Weyant et al. [50]	292 dentate women (average age 75.5 years)	Cross-sectional	OR: 1.56 [95% CI: 0.98-2.02]	No statistically significant association between periodontal disease and sys-temic BMD
Lundstrom et al. [51]	15 women with osteo-porosis, 41 women with normal BMD	Cross-sectional	OR: 1.3 [95% CI: 0.98-1.02]	No statistically significant differences in gingival bleeding, probing pocket depths, gingival recession and marginal bone level

[54] and several cytokines implicated in bone resorption [38]. Estrogen deficiency increases IL-6 concentrations in bone marrow [55,56], serum [55,57] and gingival [58] cooperatively stimulating osteoclast bone resorption.

Genetic factors that predispose a person to systemic bone loss

These also influence or predispose an individual to periodontal destruction.

Environmental factors

Such as cigarette smoking and sub optimal calcium intake, among others, may put individuals at risk for development of both osteoporosis and periodontal disease.

Osteoporosis and Dental Prosthesis

Bone loss due to osteoporosis may become so severe that it

Table 3 Risk factors for osteoporosis and periodontal disease and common risk factors.

Risk factor for Osteoporosis	Common risk factor	Risk factors for periodontal disease
Female Gender	Cigarette smoking	Plaque
Caucasian or Asian race	Nutritional deficiency	Diabetes
Hereditary	Increased age	Hormone changes
Menopause or amenorrhea	Corticosteroid use	Medical disorder
High intake of protein, caffeine, salt	Immune dysfunction	Osteoporosis
Low intake of calcium and vitamin D	-	-
Excessive alcohol	-	-
Physical inactivity	-	-
Low skeletal mass	-	-
Medical disorder	-	-

may become impossible to create functional dentures. Without the aid of dentures to chew many types of food, older patients may suffer severe nutritional deficiencies. In addition, ill-fitting dentures can lead to mouth sores and difficulty while speaking. Osteoporosis has also been suggested as a risk factor in dental implant failure, but data supporting such a link are limited [59].

Osteoporosis and Temporomandibular Disorders

Habits and conditions that provoke development of general bone loss in the skeleton may disturb the functional harmony of the masticatory system and thus may increase the possibility of temporomandibular disorders [60]. Gruber and Gregg suggested that early detection and anti resorptive therapy for osteoporosis merit future consideration in temporomandibular disorder therapy [61].

Radiographic Appearance of Osteoporotic Jaws

Cortex at the mandible angle gets distinctly thinner in postmenopausal osteoporotic women. Cortical bone cannot be seen well at the anterior margin of ramus and in the maxilla and is minimal along the alveolar crest [62].

Oral Implications of Osteoporosis Therapy

Several medications are available to increase BMD, which include hormone replacement therapy, bisphosphonates (BPs), calcitonin, selective estrogen receptor modulators, recombinant human parathyroid hormone or combination of these medications [19].

There is sufficient evidence in the literature to demonstrate that most of the medications used for the treatment and prevention of osteoporosis have the potential to reduce systemic as well as oral bone loss [14]. It has been shown that estrogen used in hormone replacement therapy of postmenopausal women is associated with reduced gingival inflammation and a reduced frequency of gingival attachment loss in osteoporotic women in early menopause [16].

Bisphosphonates (Bp) Therapy

BPs are the standard of care for increasing or maintaining bone

mass and reducing excessive bone turnover, and they have proven to be effective in reducing osteoporosis complications [63]. By inhibiting osteoclast-mediated bone resorption, BPs contribute to an increase in BMD and lead to a marked reduction in the risk of bone fractures [64,65]. They have also been shown to inhibit tumor cell proliferation and inhibit angiogenesis. These added features have made BPs useful in the management of bone metastases [66].

Two routes of administration of the drug are commonly used, oral and intravenous. BPs act almost exclusively on bone when administered at physiological doses because of specific affinity to bone, where they deposit both in newly formed bone and in proximity to the osteoclasts. The half-life of BPs in the circulation is quite short, ranging from 30 minutes to 2 hours [67]. However, once incorporated into bone tissue, they can persist for up to 10 years, depending on the skeletal turnover time [68]. Oral BPs are commonly used in the treatment of osteoporosis, Paget's disease and osteogenesis imperfecta, whereas the intravenous BPs are used in the treatment of osteolytic tumors, hypercalcemia of malignancy, multiple myeloma, bone metastases from solid tumors and other tumors [63,69]. The most common oral BPs are alendronate, risedronate and ibandronate.

BPs can both decrease osteoclast activity and decrease osteoclast numbers. The first is exemplified by internalization by osteoclasts, causing disruption of osteoclast-mediated bone resorption [70], and the second by inhibiting osteoclast recruitment and accelerating programmed cell death (apoptosis) of osteoclasts, thus reducing osteoclast numbers. Both mechanisms lead to reduction of bone resorption and to a decrease in bone turnover [71]. BPs bind avidly to exposed bone mineral around the resorbing osteoclasts, which results in very high levels of BPs in the resorption lacunae. Because bone-incorporated BPs are not metabolized, these high concentrations are maintained within bone for long periods [70].

Bisphosphonates Related Osteonecrosis of the Jaw (Bronj)

BRONJ is defined as a condition characterized by nonhealing exposed necrotic bone in the mandible or maxilla persisting for more than eight weeks in a patient who has taken or is currently taking a bisphosphonates and who has no history of radiation

therapy on the jaws [72,73]. Incidents of osteonecrosis of the jaw have been reported in persons using bisphosphonates and undergoing invasive dental treatment procedures, including tooth extractions, dental implants and surgical and nonsurgical periodontal treatment [13].

Although BPs have been reported to cause oral mucosal alterations [74,75], the changes occurring in the jawbones are of a greater significance to the dentist. BRONJ is a serious oral complication occurring in 1.8% to 12.8% of the cases with intravenous BP administration [70,76]. However, the rate of occurrence of this complication and the factors that predispose to its occurrence are not well understood. A true cause and effect relationship between osteonecrosis of the jaw and BP use has not yet been established. Most of the reported cases (95%) have been associated with zoledronic acid or pamidronate given intravenously to control metastatic bone disease [77,78]. Osteonecrosis of the jaw has developed far less often among patients who have received oral BPs at the lower doses used for osteoporosis than among patients who received the higher doses used for metastatic cancer. Even though the exact incidence of BRONJ is unknown, reports have estimated it to be about 1 in 10,000 for intravenous use of BPs. There is also an incomplete understanding of how BP therapy may affect tissue healing and the success rate of dental implants [79,80].

The mechanism by which BPs may cause or promote the occurrence of osteonecrosis of the jaws remains uncertain [81]. The potent BP-mediated inhibition of osteoclastic function leads to decreased bone resorption and inhibits normal bone turnover remodeling, resulting in areas of microdamage, accumulation and a reduction in some mechanical properties of the bone [82]. The mandible and maxillary bones normally offer a high level of resistance to infection by oral microorganisms during dental infections or extractions or when a foreign body (eg, an implant) is inserted. This resistance to infections, together with an ability to heal rapidly, is thought to stem in part from the high blood flow that characterizes the mandibular and maxillary bone [83].

Clinical features

Clinically, BRONJ presents as an area of exposed alveolar bone that occurs spontaneously or becomes evident following an invasive surgical procedure such as extraction of a tooth, periodontal surgery, apicoectomy, or dental implant placement [77]. The three most common sites for BRONJ are (1) non healing dentoalveolar sites; (2) traumatized tori (palatal and/or mandibular) and (3) exposures of portions of the mylohyoid ridge.

In a review of reported cases of BRONJ, it was found that 65% of cases involved the mandible only, 26% involved the maxilla only and 9% involved both the jaws [84]. There was a slight female predilection of 3:2. Multifocal or bilateral involvement was more common in the maxilla than in the mandible. Most of the reported lesions were on the posterior lingual aspect of the mandible near the mylohyoid ridge.

Among the reviewed cases, 60% occurred after tooth extraction or dentoalveolar surgery. Symptoms may occur spontaneously in

the bone or at the site of previous tooth extraction. Symptoms include pain, soft tissue swelling, infection secondary to dead bone, loosening of teeth and, in some cases, the ragged bone surfaces cause ulceration of the contacting soft tissues. There are associated sinus tracts, and in severe cases, a cutaneous fistula may develop. A typical lesion begins in the alveolar bone and occurs more frequently in mandibular than maxillary sites by the ratio of 2:1 [85].

Radiographically, osteolytic changes are frequently seen and the bone lesion may appear less or more radiodense than the unaffected bone, providing a radiographic appearance similar to that observed in bone metastasis. The disease can result in a long-term debilitating condition. Advanced cases of BRONJ have developed pathological fractures especially in edentulous patients with long-standing oral implants [86].

Dental treatment seems to be a precipitating event in the development of most cases of BP-related osteochemonecrosis. It is therefore imperative that osteoporosis patients for whom BP therapy is being contemplated should have their dental status assessed prior to initiation of the BP therapy. This includes control of dental caries and periodontal disease, avoiding dental implant placement, using soft liners on dentures and to recommend an alternative to tooth extractions for patients with history of receiving BP therapy. This is because withdrawal of BP therapy before major dental procedures does not appear to hasten recovery of osteonecrosis due to their persistence in bone [85].

Conclusion

The effect of osteoporosis on both oral and general health needs to be well understood. As a health care provider, the dentist could serve as a pre screener of patients with the potential for osteoporosis. Familiarity with the risk factors could aid in identifying these individuals and help in earlier diagnosis. Many of the studies conducted to date suggest there is a relationship between osteoporosis and oral health but these studies have been plagued by relatively small sample sizes and lack of adequate control of potential confounding variables such as gender, hormone intake, smoking, race, age, stress and distress, diet, body mass and exercise. A growing body of literature has been restricted to postmenopausal women regarding the role of estrogen deficiency in the onset and progression of periodontal disease. There is consistency of results of most studies, suggesting that an association likely does exist, but whether there is a causal nature to that association is not firmly established. Moreover, available scientific data suggest that patients with osteoporosis who are on bisphosphonates require special care during dental treatment, especially in regard to dental implants, due to a risk of occurrence of bisphosphonates related osteonecrosis of the jaw. Further studies are needed to assess the role of osteoporosis in various oral conditions, to determine the clinical implications of osteoporosis therapies on oral health and to elucidate whether dental examination might be of value for initial screening for signs of osteoporosis.

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