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

Ioanna Skoufou¹, Maria Yavropoulou², Christos Zafeiris¹,³

¹Postgraduate Program “Metabolic Bone Diseases”, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece; ²Division of Endocrinology and Metabolism, 1st Propaedeutic Department of Internal Medicine LAIKO General Hospital of Athens, National and Kapodistrian University of Athens, Greece; ³Laboratory for Research of Musculoskeletal System “Theodoros Garofalidis”, University of Athens, KAT Hospital, Athens, Greece

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 margin¹. This periodontal infection leads to alveolar bone loss and eventually tooth loss, if left untreated². 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 infection³. 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 infection⁴,⁵. 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 treatment⁶. This aspect is firmly noticed among postmenopausal women, who frequently suffer from both osteolytic conditions⁷. 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 maladies⁸. 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 osteoporosis⁹.

Common risk factors and comorbidities

Periodontitis has often been reported as a systematic disease independently associated with a range of...
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\(^\text{10}\).

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\(^\text{11-14}\). The underlying mechanism of the precedent correlation includes sex hormones and blood nutrients deficiency, as well as, the accumulation of Reactive Oxygen Species (ROS)\(^3\).

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-β-carotene folate and vitamin D, which are frequently observed in elderly, might be involved in the relationship between aging and periodontal disease\(^\text{15,16}\). The maintenance of serum 25(OH)D levels within normal range modulates a patient’s respond to periodontal treatment\(^\text{16,17}\). 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\(^\text{22}\). Insufficient calcium intake has been correlated with periodontal disease mainly through its impact on bone metabolism\(^\text{33}\). 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\(^\text{14}\).

2) **Smoking:** Smoking has been firmly associated independently with osteoporosis by a plethora of studies\(^\text{16,17}\). 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\(^\text{18}\). 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)\(^\text{19}\), 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)\(^\text{20}\). 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\(^\text{21}\).

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\(^\text{22}\). 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\(^\text{23}\). Smokers also respond less favorably than non smokers to periodontal treatment\(^\text{22}\). However, participating in cessation programs, not only will ameliorate their response to therapy, but will also reverse many tobacco effects on periodontal tissues\(^\text{24}\).

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\(^\text{25,26}\). 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\(^\text{27}\). Vitamin D deficiency (serum 25(OH)D<20 ng/ml) is significantly associated with diminished bone mineral density and osteoporotic fractures\(^\text{28}\), while people, especially the elderly, are often presented with low dietary calcium intake, enhancing the release of this mineral from bones through resorption\(^\text{29,30}\).

Through its’ crucial position in bone metabolism and anti-inflammatory activity, vitamin D affects periodontal status as well. The maintenance of serum 25(OH)D levels within normal range modulates a patient’s respond to periodontal treatment\(^\text{16,17}\). 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\(^\text{22}\). Insufficient calcium intake has been correlated with periodontal disease mainly through its impact on bone metabolism\(^\text{33}\). 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\(^\text{14}\).

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 α (TNF-α). These cytokines induce bone resorption which, in turn reduces the excretion of parathyroid hormone (PTH). As a consequence, 1,25(OH)\(_2\)D\(_3\) production diminishes and compromises calcium intestinal absorption, a condition that aggravates bone resorption\(^\text{3,6}\).

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\(^\text{35,36}\).

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\(^\text{37,38}\). 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\(^\text{37}\). 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, IL 10 and vitamin D receptor38.

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 organism39. Researches have proved that ROS affect negatively the Wnt/β-catenin pathway, reducing osteoblastogenesis and subsequently promoting bone resorption and reducing bone mass3,40.

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 ROS41. Moreover, ROS, especially H2O2, induce the apoptosis of periodontal ligament cells, via mitochondrial abnormalities, a fact which defines oxidative stress as an independent risk factor for periodontitis42.

**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 osteoporosis43. 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 significantly great 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 women44. 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 periodontitis45. 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 BMD46. 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)47. 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 periodontitis48. 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 gender49.

**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 risk50. 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 osteoporosis51. 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 osteoporosis52. 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 status53.

**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.54. 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 osteoporosis55. 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 osteoporosis51.56. 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 pathways56.

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 symptoms57. 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.

References

1. Lindhe J, Lang NP, Karring T. Clinical periodontology and implant dentistry. 5th edition 2008 Blackwell Publishing Ltd.
2. Mantzavinos ZS, Vrotsos IA. Clinical periodontology. 2002 Litsas, Athens.
3. Lyntis GP. Bone metabolic diseases. 5th edition 2013 Hylonome, Athens.
4. Šavić Pavičić I, Dumančić J, Jukić T, Badel T. The relationship between periodontal disease, tooth loss and decreased skeletal bone mineral density in ageing women. Gerontology 2017; 34(4):441-445.
5. Wactawsky-Wende J. Periodontal diseases and osteoporosis: association and mechanisms. Annals periodontology 2001; 6(1):197-208.
6. Wang CJ, McCauley UK. Osteoporosis and periodontitis. Current osteoporosis reports 2016; 14(6):284-291.
7. Straka M, Straka-Trapezanlidis M, Degjovic J, Varga I. Periodontitis and osteoporosis. Neuro endocrinology letters 2015;36(5):401-6.
8. Lapérine O, Cloitre A, Caillon J, Huch B, Bugueno IM, Pilet P, Sourice S, Le Tilly E, Palmer G, Daviaud JL, Geoffroy V, Guicheux J, Beck-Cornnier S, Lescous P. Interleukin-33 and RANK-L Interplay in the Alveolar Bone Loss Associated to Periodontitis. PLoS One 2016; 11(12):e0168080.
9. Marshalkar VN, Suragamath G, Zope SA, Varma SA. A Cross-Sectional Study to Assess and Correlate Osteoporosis and Periodontitis among Postmenopausal Women. A Dual Energy X-Ray Absorptiometry Study. Journal of mid-life health 2018;9(1):2-7.
10. Holmstrup P, Damgaard C, Olsen I, Kline B, Flyverborg A, Nielsen CH, Hansen PR. Comorbidity of periodontal disease: two sides of the same coin? An introduction for the clinician. Journal of oral microbiology 2017;9(1):1332710.
11. Tarantino U, Iolascon G, Gianferotti L, Masi L, Marucci G, Giusti F, Marni F, Parri S, Feola M, Rao C, Piccioni E, Zanetti EB, Citadini N, Alvaro R, Moretti A, Calafiore D, Toro G, Gmigiano F, Resmini G, Brandi ML. Clinical guidelines for the prevention and treatment of osteoporosis: summary statements and recommendations from the Italian Society for Orthopaedic Traumatology. Journal of orthopaedics and traumatology 2017;18(Suppl 1):3-36.
12. Compston J, Cooper A, Cooper C, Otgoes N, Gregson C, Harvey N, Hope S, Kanis JA, McCloskey EV, Poole KES, Reid DM, Selby P, Thompson F, Thurston A, Vine N, National Osteoporosis Guideline Group (NOGG) UK clinical guideline for the prevention and treatment of osteoporosis. Archives of osteoporosis 2017;12(1):43.
13. Cosman F, de Beur SJ, LeBoff MS, Lewiecki EM, Tanner B, Randall S, Lindsay R. National Osteoporosis Foundation Clinician’s Guide to Prevention and Treatment of Osteoporosis. Osteoporosis international 2014;25(10):2359-81.
14. Svedbom A, Hemlund E, Ivergård M, Compston J, Cooper C, Stenmark J, McCloskey EV, Jonsson B, Kanis JA; EU Review Panel of IOF. Osteoporosis in the European Union: a compendium of country-specific reports. Archives of osteoporosis 2013;8(1):137.
15. Wellapuli N, Ekanayake L. Risk factors for chronic periodontitis in Sri Lankan adults: a population-based case-control study. BMC medical notes 2017;10(1):460.
16. Ebersole JL, Lambert J, Bush H, Hija PE, Basu A. Serum Nutrient Levels and Aging Effects on Periodontitis. Nutrients 2018;10(12).
17. Biclic J, Milicevic S, Balaban J. Risk Factors for Osteoporosis in Postmenopausal Women. Medical archives 2017;71(1):25-28.
18. Baccaro LF, Conde DM, Costa-Paiva L, Pinto-Neto AM. The epidemiology and management of postmenopausal osteoporosis: a viewpoint from Brazil. Clinical interventions in aging 2015;10:583-91.
19. González J, Rodríguez-Fraile M, Rivera P, Restituto P, Colina I, Calleja MLD, Alcaide AB, Campo A, Bértó J, Seijo LM, Pérez T, Zulueta J, Víaro N, de-Torres JP. Trabecular bone score in active or former smokers with and without COPD. PLoS One 2019;14(2):e0209777.

20. Ghadimi R, Hosseini SR, Asefi S, Bijaee A, Hoidari B, Babaei M. Influence of Smoking on Bone Mineral Density in Elderly Men. International journal of preventive medicine 2018;9:11.

21. Juonala M, Pitkänen N, Tolonen S, Laaksonen M, Sievänen H, Jokinen E, Laatikainen T, Sabin MA, Hutri-Kahonen N, Heikinheimo K, Taattonen L, Jula A, Loo BM, Imviraara O, Kähönen M, Magnusson CG, Viikari JS, Raitakari OT. Childhood exposure to passive smoking and bone health in adulthood. The Cardiovascular Risk in Young Finns Study. The journal of clinical endocrinology and metabolism 2019 Feb 1. doi: 10.1210/jc.2018-02501.

22. Nociti FH. Jr, Casati MZ, Duarte PM. Current perspective of the role of vitamin D in the human body with a special emphasis on dental issues: Literature review. Dental and medical problems 2018;55(4):419-424.

23. Krawiec M, Dominiak M. The role of vitamin D in the human body with a special emphasis on dental issues: Literature review. Dental and medical problems 2018;55(4):419-424.

24. Lips P, Cashman KD, Lamberg-Allardt C, Bischoff-Ferrari HA, O’Connor-Pietsch BR, Bianchi M, Stapan J, El-Haj Fuleihan G, Bouillon R. Management of endocrine disease: Cur-rent vitamin D status in European and Middle East countries and strategies to prevent vitamin D deficiency; a position statement of the European Calcified Tissue Society. European journal of endocrinology 2019 Feb 1. pii: EJE-18-0736.R1. doi: 10.1530/EJE-18-0736.

25. Weaver CM, Alexander DD, Boushey CJ, Dawson-Hughes B, Lappe JM, LeBoff MS, Liu S, Looker AC, Wallace TC, Wang DD. Calcium plus vitamin D supplementation and risk of fractures: an updated meta-analysis from the National Osteoporosis Foundation. Osteoporosis international 2016;27(1):367-76.

26. Lips P, Cashman KD, Lamberg-Allardt C, Bischoff-Ferrari HA, O’Connor-Pietsch BR, Bianchi M, Stapan J, El-Haj Fuleihan G, Bouillon R. Management of endocrine disease: Cur-rent vitamin D status in European and Middle East countries and strategies to prevent vitamin D deficiency; a position statement of the European Calcified Tissue Society. European journal of endocrinology 2019 Feb 1. pii: EJE-18-0736.R1. doi: 10.1530/EJE-18-0736.

27. Fang A, Li K. Calcium deficiency: where does the diagnostic criterion come from and by what is bone health influenced? Chinese medical journal 2014;127(24):4161-3.

28. Bolland MJ, Grey A, Reid IR. Should we prescribe calcium or vitamin D supplements to treat or prevent osteoporosis? Climacterics 2015; 18 Suppl 2:22-31.

29. Krawiec M, Dominiak M. The role of vitamin D in the human body with a special emphasis on dental issues: Literature review. Dental and medical problems 2018;55(4):419-424.

30. Krawiec M, Dominiak M. The role of vitamin D in the human body with a special emphasis on dental issues: Literature review. Dental and medical problems 2018;55(4):419-424.

31. Krawiec M, Dominiak M. The role of vitamin D in the human body with a special emphasis on dental issues: Literature review. Dental and medical problems 2018;55(4):419-424.

32. Krawiec M, Dominiak M. The role of vitamin D in the human body with a special emphasis on dental issues: Literature review. Dental and medical problems 2018;55(4):419-424.

33. Krawiec M, Dominiak M. The role of vitamin D in the human body with a special emphasis on dental issues: Literature review. Dental and medical problems 2018;55(4):419-424.

34. Kim HS, Kim YY, Oh JK, Bae KH. Is yogurt intake associated with periodontitis due to calcium? PLoS One 2017;12(10):e0187258.

35. Shapiro LF, Freeman K. The relationship between estrogen, estrogen receptors and periodon-tal disease in adult women: a review of the literature. The New York state dental journal 2014;80(3):30-4.

36. Lee DJ, Wu L, Shimono M, Piao Z, Green DW, Lee JM, Jung HS. Differential Mechanism of Periodontitis Progression in Postmenopause. Frontiers in physiology 2018;9:1098.

37. Greenhill C. Unravelling the genetics of osteoporosis. Nature reviews. Endocrinology 2019;15(3):129.

38. Stabholz A, Sokolove WA. Shapiro L. Genetic and environmental risk factors for chronic peri-dontitis and aggressive periodontitis. Periodontology 2000 2010;53:138-53.

39. Pizzino G, Imura N, Cucinotta M, Palillo G, Mannoni F, Arcoraci V, Squadrino F, Altavilla D, Bitto A. Oxidative Stress. Harms and Benefits for Human Health. Oxidative medicine and cellular longevity 2017;18:416763. doi: 10.1155/2017/18:416763.

40. Zhou Q, Zhu L, Zhang D, Li N, Li Q, Dai P, Mao Y, Li X, Ma J, Huang S. Oxidative Stress-Related Biomarkers in Postmenopausal Osteoporosis: A Systematic Review and Meta-Analyses. Disease markers 2016;7067984. doi: 10.1155/2016/7067984.

41. Wang Y, Andrukhov O, Rausch-Fan X. Oxidative Stress and Antioxidant System in Periodontitis. Frontiers in physiology 2017;8:910.

42. Chen Y, Ji Y, Jin X, Sun X, Zhang X, Chen Y, Shi L, Cheng H, Mao Y, Li X, Hou Y, Zhang D, Zhao S, Ma J, Huang S. Mitochondrial abnormalities are involved in periodontal ligament fibroblast apoptosis induced by oxidative stress. Biochemical and biophysical research communications 2019;509(2):483-490.

43. Wada-Mihara C, Seto H, Ohtba H, Tokunaga K, Kido JI, Nagata T, Narushi K. Local adm-inistration of calcitonin inhibits alveolar bone loss in an experimental periodontitis in rats. Biomedicine & pharmacotherapy 2018;97:765-770.

44. Ayed MS, Alsharif AF, Divakar DD, Jhugroo C, Aboaim B, Mustafa M. Evaluating the pos-sible association between systemic osteoporosis and periodontal disease progression in postmenopausal women. Disease-a-month 2018 Nov 27. pii: S0011-5029(18)30151-2. doi: 10.1016/j.disamonth.2018.11.OO1.

45. Penoni DC, Fidalgo TK, Torres SR, Varela VM, Masterson D, Leão AT, Maia LC. Bone Den-sity and Clinical Periodontal Attachment in Postmenopausal Women: A Systematic Review and Meta-Analysis. Journal of dental research 2017;96(3):261-269.

46. Richa R Y, Puranik MP, Shrivastava A. Association between osteoporosis and periodontal disease among postmenopausal Indian women. Journal of investigative and clinical dentistry 2017;8(3).

47. Juluri R, Prashanth E, Gopalakrishnan D, Kathariya R, Devanooorkar A, Viswanathan V, Romansen G. Association of Postmenopausal Osteoporosis and Periodontal Disease: A Dou-ble-Blind Case-Control Study. Journal of international oral health 2015;7(9):119-23.

48. Kim CS, Kim AK, Lee KS, Lee HK, Choi YH, Hwang TY, Moon JS. Relationship between bone mineral density, its associated physiological factors, and tooth loss in postmenopausal Korean women. BMC womens health 2015;15:65.

49. Jang KM, Cho KH, Lee SH, Han SB, Han KD, Kim YH. Tooth loss and bone mineral densi-ty in postmenopausal South Korean women. Journal of investigative and clinical dentistry 2015;7(8):3.

50. Choi JK, Kim YT, Kweon HI, Park EC, Leão AT, Maia LC. Bone Den-sity and Clinical Periodontal Attachment in Postmenopausal Women: A Systematic Review and Meta-Analysis. Journal of dental research 2017;96(3):261-269.

51. Kolte RA, Kolte AP, Potey AM. Risk assessment of osteoporosis among postmenopausal women. Indian journal of dental research 2017;28(4):388-394.

52. Krolle RA, Kolte AP, Potey AM. Risk assessment of osteoporosis in pre- and postmenopausal peri-don tally healthy and chronic periodontitis women with digital panoramic radiographs. Journal of indian society of periodontology 2017;21(6):461-465.
Cheng WC, Huang RY. Patients with chronic periodontitis present increased risk for osteoporosis: A population-based cohort study in Taiwan. Journal of periodontal research 2017;52(5):922-929.

53. Lee JH, Oh JY, Youk TM, Jeong SN, Kim YT, Choi SH. Association between periodontal disease and non-communicable diseases: A 12-year longitudinal health-examinee cohort study in South Korea. Medicine (Baltimore) 2017;96(26):e7398.

54. Baldodia A, Sharma RK, Tewari S, Narula SC. Effect of periodontitis on bone mineral density in postmenopausal women: A non-randomized interventional study. Quintessence international 2017;48(2):113-122.

55. Huang YF, Chang CT, Liu SP, Muo CH, Tsai CH, Hong HH, Shen YF, Wu CZ. The Impact of Oral Hygiene Maintenance on the Association Between Periodontitis and Osteoporosis: A Nationwide Population-Based Cross Sectional Study. Medicine (Baltimore) 2016;95(6):e2348.

56. Reddy MS, Morgan SL. Decreased bone mineral density and periodontal management. Periodontology 2000 2013;61(1):195-218.

57. Palomo L, Chitguppi R, Buencamino MC, Santos D, Thacker H. A need to educate post-menopausal women of their periodontal health. Journal of Indian society of periodontology 2013.