

# Osteoporosis and Periodontitis in Postmenopausal Women: A Systematic Review

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**ABSTRACT**

This systematic review was done to assess the strength of association between osteoporosis and chronic periodontitis in postmenopausal women, assessed by bone mineral density (BMD) and clinical attachment loss, respectively. The Pubmed, Cochrane central, EMBASE, and Google Scholar were searched from year 1990 to 2015 for studies on association between chronic periodontitis and osteoporosis. Studies measuring osteoporosis in terms of central BMD and periodontitis in terms of clinical attachment level were studied. Data were extracted and descriptive analysis was performed. Screening of 1188 articles resulted in 24 articles for review after reading the titles and abstracts. Fifteen studies were shortlisted for inclusion in systematic review. Ten of these studies showed an association between periodontitis and osteoporosis. It implies that patients with severe periodontitis should also be evaluated for systemic bone health and vice versa.

**KEYWORDS:** Bone mineral density, chronic disease, inflammation, tooth loss

## INTRODUCTION

Chronic periodontitis is characterized by loss of periodontal attachment due to destruction of the periodontal ligament and loss of the adjacent supporting bone.<sup>[1]</sup> The epidemiology of periodontitis is complicated by the varying definitions of the disease and widely reported global variations in the prevalence and severity of the disease.<sup>[2,3]</sup> Several host factors are responsible for progression of the periodontal disease such as smoking, diabetes mellitus, obesity, steroids, or cytotoxic medications.<sup>[4]</sup> Prevalence of periodontitis increases with age and is the most common cause of tooth extraction in older patients.<sup>[5]</sup> Postmenopausal status is also an important risk factor for periodontal diseases.<sup>[6,7]</sup>

Osteoporosis is decreasing bone mass with weakening of microarchitecture of the bone. According to the World Health Organization (WHO) criteria, osteoporosis is defined as a bone mineral density (BMD) that lies 2.5 standard deviations or more below the average value for young healthy women. Normal BMD is defined as *T*-score of  $-1.0$  or higher and a *T*-score between  $-1.0$  and  $-2.5$  is defined as osteopenia or low bone mass.<sup>[8]</sup> Elderly postmenopausal females are worst affected

by osteoporosis.<sup>[9]</sup> Since both these conditions share common risk factors and loss of supporting periodontal bone is associated with progression of periodontitis, various researchers have looked into association between the two conditions.<sup>[10-34]</sup>

Both chronic periodontitis and osteoporosis are slowly developing diseases that often come to notice only after a significant amount of damage has already taken place. Pharmacotherapy and dietary interventions are an effective means of prevention of postmenopausal osteoporosis.<sup>[35]</sup> Understanding the association between osteoporosis and chronic periodontitis could be useful if their prevention and treatment are inter-related. Although there is some evidence on the association between osteoporosis and periodontitis, no study has summarized these findings. The aim of this review was to systematically review the literature to determine if there is an association between chronic periodontitis and osteoporosis.

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## MATERIALS AND METHODS

This systematic review was conducted in accordance with the 2009 PRISMA statement.<sup>[36]</sup>

**Focused Question:** Is there an association between osteoporosis and periodontitis in postmenopausal women, as assessed by BMD and clinical attachment loss, respectively?

### Search strategy

Comprehensive search of literature was carried out using PubMed (<http://www.ncbi.nlm.nih.gov/pubmed>), EMBASE (<http://www.elsevier.com/online-tools/embase>), Google Scholar, and the Cochrane database (<http://www.cochrane.org>) for all studies published in the English language before 24<sup>th</sup> December 2015. The following search terms were used: (“osteoporosis” [MeSH] OR “bone density” [MeSH]) AND (“periodontitis” [MeSH] OR “periodontal attachment loss” [MeSH] OR “periodontal”). The eligible studies were selected by going through the title and abstracts. Full text was extracted for the studies found eligible after study of abstracts. The references of the studies shortlisted for review and articles found in this search were hand searched.

### Screening and selection

#### Inclusion criteria

1. Studies on human subjects published in English language were included for the review
2. Studies that were of case-control or cohort or cross-sectional designs. Studies were included if they directly compared the association between osteoporosis (expressed in terms of BMD) and chronic periodontitis measured in terms of clinical attachment level (CAL) or CAL and pocket probing depth (PPD)
3. Diagnosis of osteoporosis made using dual energy X-ray absorptiometry (DEXA) test performed on hip or spine
4. Postmenopausal females were included for study.

#### Exclusion criteria

1. Review articles and case series were excluded
2. DEXA on peripheral bones or diagnosis of osteoporosis using ultrasonography or X-rays was excluded as these do not give as accurate diagnosis of osteoporosis as DEXA of axial skeleton
3. Studies where diagnosis of chronic periodontitis was made using tooth loss, oral hygiene, gingival appearance, or use of a dental prosthesis were excluded
4. Studies based on self-reported diagnosis of osteoporosis/periodontal conditions were also excluded

5. Studies that did not report any estimates for the association between osteoporosis and periodontitis were excluded.

### Definition of osteoporosis and periodontitis

The WHO definition of osteoporosis, where osteoporosis is defined in terms of *T*-score of the BMD was taken.<sup>[8]</sup> Osteoporosis is diagnosed when the *T*-score is 2.5 standard deviations or more below the mean BMD value of a young sex-matched reference population. Studies which had calculated BMD on both the lumbar spine and hip, we took the values of the worst affected site. Periodontitis was defined by criteria given by American Academy of Periodontology, patients having  $\geq 3$  mm of clinical attachment loss and more than 30% of sites involved.<sup>[1]</sup> Periodontitis was expressed in terms of measured values of CAL or CAL and PPD.

### Data collection

From each eligible study, following information was extracted: First author, year of publication, study design, country, ethnicity of population, mean age, gender, sample size, BMD site, *T*-scores, CAL, PPD, and relevant effect sizes (mean difference, odds ratios or relative risks, or correlation coefficients). Screening of abstracts and full texts and data extraction were performed independently by two different reviewers (LG and TG). If there was any discrepancy between the reviewers it was resolved by mutual consensus.

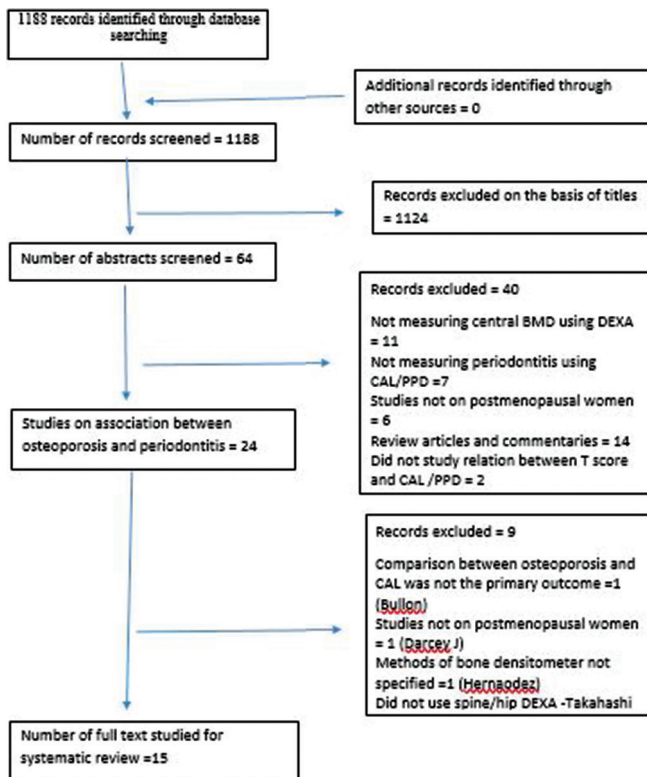
### Statistical methods

The studies were heterogeneous in terms of cutoff values of CAL used for diagnosis of severe periodontitis. There were differences in the statistical analysis and reporting of results so that data from these studies could not be pooled together for a meta-analysis.

## RESULTS

Initial search showed 1188 articles, of which 723 were in English language and on human subjects. Of these, 24 articles were selected for further review after reading the titles and abstracts.<sup>[9-32]</sup> Full texts of these articles were extracted, and on the basis of inclusion criteria mentioned before, 15 studies were shortlisted for inclusion in systematic review.<sup>[11-25]</sup> The details of the study selection process are shown in Figure 1. All included studies were case-control or cross-sectional in nature, with level IV evidence.<sup>[37]</sup>

A total number of patients in these studies were 4210. Demographic details and chief conclusion from the studies are summarized in Table 1. Most of the included studies had expressed the results in different statistical terms such as mean values of CAL in different groups, correlation or regression coefficients, and odds ratio [Tables 2-4]. Cutoff



**Figure 1:** PRISMA flowchart describing the process of study selection and exclusion

values for CAL and PPD were different in different studies [Table 1]. Among the 15 studies included in the systematic review, ten showed a significant association between chronic periodontitis and osteoporosis.

Brennan *et al.*<sup>[11]</sup> had used the highest sample size of 1329 patients. They found significant correlation for worst site *T*-score ( $r = -0.069$ ,  $P = 0.01$ ) and BMD of total forearm ( $-0.092$ ,  $P = 0.001$ ), anteroposterior spine ( $r = -0.058$ ,  $P = 0.05$ ), and whole body ( $r = -0.056$ ,  $P = 0.048$ ).

## DISCUSSION

This systematic review favors a strong association between the central BMD and CAL. Periodontitis is infection-induced inflammation of the structures around the tooth resulting in loss of its soft tissue attachment and surrounding bone mass, finally resulting in tooth loss. Not only local factors such as hygiene are associated with periodontitis, systemic factors such as diabetes, smoking, and poor general health but also affect periodontal status. A relation between osteoporosis and periodontitis has also been postulated in literature, which is also supported by this systematic review. Osteoporosis being a systemic disease, leads to loss of bone stock not only from spine and appendicular skeleton but also from the alveolar bone.<sup>[38]</sup> Thus, osteoporosis is expected to hasten the process of bone loss in chronic periodontitis.<sup>[39]</sup>

Osteoporosis is well known in postmenopausal women with maximum bone loss occurs in the first 5 years following menopause.<sup>[40]</sup> Both osteoporosis and chronic periodontitis are slowly progressive diseases sharing many features together. Osteoporosis is well known in postmenopausal women with prevalence as high as 50%.<sup>[41,42]</sup> Postmenopausal status is also associated with increased severity of periodontitis with prevalence as high as 30%.<sup>[43,44]</sup> Osteoporosis is a silent killer and osteoporosis-related fractures contribute to significant amount of morbidity and mortality in older population.<sup>[45]</sup> Chronic periodontitis has also been associated with increased mortality in older patients, as it may be an indicator of several associated chronic illnesses and ill health.<sup>[46]</sup>

Periodontitis is chronic inflammatory disease of supporting structures of teeth which is measured in terms of CAL, PPD, and alveolar bone loss. We selected the studies which includes CAL or CAL and PPD both. CAL is a better indicator of chronic periodontitis compared to other indicators such as number of missing teeth, PPD, and alveolar crestal height (ACH). PPD is most commonly used indicator for periodontitis, but it also measures gingiva coronal to cemento-enamel junction. ACH has to be measured using oral radiographs and thus may depend on the quality and angle of X-ray projection. CAL can be measured clinically and will appear earlier compared to radiographic changes. Further generalized loss of bone density with osteoporosis may directly affect the alveolar bone.

Studies which had calculated BMD on both the lumbar spine and hip were included. Central or axial BMD, measured at spine or hip, is the most sensitive marker of osteoporosis, compared to peripheral BMD measurement at sites such as wrist or calcaneum. There is poor association between peripheral BMD and future fracture risk and the definition of osteoporosis based on peripheral BMD values are unreliable.<sup>[47]</sup> Brennan *et al.*<sup>[11]</sup> studied 1329 participants and found significant correlation between CAL and BMD of total forearm, worst site *T*-score, anteroposterior spine, and whole body. Unadjusted results of regression analysis showed consistent inverse association between BMD and CAL. However, after adjustment for age, cigarette smoking, and education, last dental cleaning results were not significant. Presence or absence of subgingival calculus was strong effect modifier. They found strongest association between BMD and clinical attachment loss in women without subgingival calculus. In the study by Tejal *et al.*,<sup>[24]</sup> there was a weak correlation between the CAL and systemic osteoporosis ( $r = 0.10-0.17$ ), which did not reach statistical significance. Four studies

**Table 1: Summary of studies included, their main finding, and conclusion**

Study (year)	Type of study	Sample size	Country of study	Mean age±SD	BMI	Criteria and cutoffs used for diagnosis of periodontitis	BMD measurement procedure	Number of patients with osteoporosis	Number of patients with periodontitis	Significant association between CAL and osteoporosis
Brennan <i>et al.</i> (2007)	CS	1329	USA	66.6±7.0	NA	CAL	DEXA spine, hip, forearm, whole body	Normal 508 (44.8%) Osteopenia 469 (41.4%) Osteoporosis 157	NA	Yes
Gomes-Filho <i>et al.</i> (2007)	CC	139	Brazil	58.8±6.4	25.5±5.1	PPD >4 mm with CAL >3 mm	DEXA femur/spine	40 cases and 60 controls	48	Yes
Gondim (2013)	CS	148	Brazil	58.93±4.7	27.61±4.80	CAL, PPD Moderate: CAL ≤5 mm Severe: CAL >5 mm	DEXA lumbar spine (L1-L4), femoral neck, and total femur	NA	NA	Yes
Grocholewicz <i>et al.</i> (2012)	CS	37	Poland	59.4±5.6	NA	PDI of 6 indicates an attachment loss of ≥6 mm	DEXA lumbar spine (L2-L4), femoral neck, and distal radius	NA	NA	Yes
Habashneh <i>et al.</i> (2010)	CS	400	Jordan	62.5±6.4	<25: 29; 25-29.9: 94; >30: 277	PPD, CAL 5 mm PD/6 mm CAL	DEXA lumbar spine (L1-L4) and femoral neck	Normal 94 (23.5%) Osteopenia 170 (42.5%) Osteoporosis 136 (34.0%)		Yes
Iwasaki <i>et al.</i> (2013)	CS	397	Japan	68.2 (60-80)	NA	CAL, PPD ≥4 mm	DEXA lumbar spine (L2-L4), femoral neck	Normal 161 (44.8%) Osteopenia 136 (41.4%) Osteoporosis 100	142 (35.8%)	Yes
Juluri <i>et al.</i> (2015)	CC	100	India	60.12	NA	CAL, PPD	DEXA lumbar spine	50 cases and 50 controls	NA	Yes
Marjanovic <i>et al.</i> (2013)	CS	380	UK	45-65	NA	PPD >5.5 mm CAL >7 mm	DEXA proximal Femur and lumbar spine	Osteoporotic 98 Nonosteoporotic 282	150	No
Moeintaghavi <i>et al.</i> (2013)	CS	60	Iran	53.05	NA	PPD, CAL	DEXA proximal Femur and lumbar spine	Normal 20 Osteopenia 20 Osteoporosis 20	NA	No
Passos <i>et al.</i> (2013)	CC	521	Brazil	60.8	NA	PPD >5 mm with CAL >6 mm	DEXA proximal Femur and lumbar spine	Osteoporosis 380 Osteopenia 141	94	Yes
Penoni <i>et al.</i> (2015)	CS	134	Brazil	69.84	28.22	PPD >5 mm with CAL >6 mm	DEXA proximal Femur, total femur and lumbar spine	Normal 48 Osteoporosis 86	51	Yes

Contd...

**Table 1: Contd...**

Study (year)	Type of study	Sample size	Country of study	Mean age±SD	BMI	Criteria and cutoffs used for diagnosis of periodontitis	BMD measurement procedure	Number of patients with osteoporosis	Number of patients with periodontitis	Significant association between CAL and osteoporosis
Pilgram <i>et al.</i> (2002)	CS	135	USA	59	NA	PPD, CAL	DEXA proximal Femur and lumbar spine	NA	NA	No
Singh <i>et al.</i> (2014)	CS	78	India	NA	26.44	PPD, CAL	DEXA lumbar spine (L1-L4)	Normal 22 Osteopenia 25 Osteoporosis 31	NA	Yes
Tejal <i>et al.</i> (2000)	CS	70	USA	62.10±7.1	25.7±5.2	CAL, ABL	DEXA proximal Femur and lumbar spine	NA	NA	No
Weyant <i>et al.</i> (1999)	CS	292	USA	75.5±4.38		PPD, CAL	DEXA proximal Femur and lumbar spine	NA	142	No

CS: Cross-sectional, CC: Case-control, NA: Information not available, PPD: Pocket probing depth, CAL: Clinical attachment level, BMD: Bone mineral density, SD: Standard deviation, PDI: Periodontal disease index, ABL: Alveolar bone level, DEXA: Dual energy X-ray absorptiometry, BMI: Body mass index

**Table 2: Summary of relation between bone mineral density and clinical attachment loss in included studies (correlation coefficients)**

Study	Sample size	Mean BMD	Mean CAL (mm)	Correlation coefficient, P	Regression analysis, β (P)
Brennan <i>et al.</i> (2007)	1329	1.05±0.11 (0.76-1.45) (whole body)	2.39±0.64 (1.16-5.22)	-0.069, 0.012	-0.071 (0.002)
Gondim <i>et al.</i> (2013)	148	0.769±0.143 (0.462-1.197)	2.78±0.09 (1.23-8.47)	-0.13, 0.231	-0.008 (0.015) Adjusted r <sup>2</sup> =0.43
Grocholewicz <i>et al.</i> (2012)	37	0.812±0.132 (0.577-1.094)	PDI instead of CAL 2.8±1.4 (0-5.4)	-0.42, 0.0398	Not stated
Iwasaki <i>et al.</i> (2013)	397	NA	NA	NA	0.003
Pilgram <i>et al.</i> (2002)	135	NA	NA	-0.03, 0.75	NA
Singh <i>et al.</i> (2014)	78	NA	3.260±0.128	-0.474, 0.000	NA
Tejal <i>et al.</i> (2000)	70	Not stated	2.7±1.0 (1.3-6.7)	-0.16, >0.05	Not stated
Weyant <i>et al.</i> (1999)	292	NA	NA	NA	P>0.05

CAL: Clinical attachment level, BMD: Bone mineral density, PDI: Periodontal disease index, NA: Not available

**Table 3: Summary of relation between bone mineral density and clinical attachment loss (odds ratio)**

Study	Number of patients with periodontitis who are osteoporotic	Number of patients with periodontitis who are nonosteoporotic	OR (95% CI)
Gomes-Filho <i>et al.</i> (2007)	NA	NA	2.58 (1.01-6.82) P=0.03
Habashneh <i>et al.</i> (2010)	74/136	104/264	2.45 (1.38-4.34) P=0.002
Iwasaki <i>et al.</i> (2013)	32/142	90/142	P=0.448
Marjanovic <i>et al.</i> (2013)	25/98 (2 sextants)	57/282 (2 sextants)	1.17 (0.67-2.05)
Passos <i>et al.</i> (2013)	74/94	20/94	P=0.01
Penoni <i>et al.</i> (2015)	NA	NA	P=0.02

OR: Odds ratio, CI: Confidence interval, NA: Not available

did not find any association between periodontitis and osteoporosis.<sup>[18,19,22,25]</sup> Marjanovic *et al.*<sup>[18]</sup> could not establish any association between osteoporosis and chronic periodontitis. Adjusted odds ratio for association

**Table 4: Summary of relation between bone mineral density and clinical attachment loss**

	BMD group	Number of patients	Mean value of CAL±SD	P
Brennan <i>et al.</i> (2007)	Normal	384	2.33±0.58	0.08
	Osteopenia	658	2.39±0.67	
	Osteoporosis	287	2.44±0.64	
Habashneh <i>et al.</i> (2010)	Normal	94	6.85±1.90	0.671
	Osteopenia	170	6.79±1.98	
	Osteoporosis	136	6.40±2.16	
Juluri <i>et al.</i> (2015)	Normal	50	3.28±0.83	0.014
	Osteoporosis	50	3.67±0.73	
Moeintaghavi <i>et al.</i> (2013)	Normal	20	1.64±0.81	0.52
	Osteopenia	20	1.42±0.67	
	Osteoporosis	20	1.44±0.50	

CAL: Clinical attachment level, BMD: Bone mineral density, SD: Standard deviation

between osteoporosis and severe periodontal disease was 0.99 (95% Confidence interval 0.61–1.61). This was a relatively larger study involving 380 participants. This was the strongest evidence against possible association between CAL and osteoporosis in this systematic review. One limitation of this study was that it measured CAL in one or two sextants only and not in the whole mouth. Furthermore, the study did not clearly mention whether premenopausal women were excluded from the study.

Pilgram *et al.*<sup>[22]</sup> found a weak positive correlation between the periodontal status and BMD in longitudinal follow-up of 3 years though no correlation could be seen at cross-sectional level in 135 participants. However, this study had some limitations. The primary objective was to study the effect of hormone replacement therapy on bone density and periodontal status. The number of patients suffering from osteoporosis or periodontitis was not revealed. Although Weyant *et al.*<sup>[25]</sup> found no statistically significant association between periodontal indicators and BMD in 292 participants, a trend toward a more severe periodontal disease was seen in all their measurements with decreasing BMD, indication of a possible association. Moeintaghavi *et al.*<sup>[19]</sup> also did not find any statistically significant association between osteoporosis and periodontitis, but the sample size was very small.

There has been a strong association in literature between loss of ACH and osteoporosis,<sup>[48]</sup> but conclusion on correlation between CAL and osteoporosis is lacking. A significant association between CAL and osteoporosis should imply that mechanisms other than systemic bone loss and reduction in alveolar bone density with osteoporosis play an important role in the development and progression of chronic periodontitis. There is an increasing evidence that osteoporosis may be a result

of systemic inflammation.<sup>[49-51]</sup> This paves way for a common mechanism for osteoporosis and chronic periodontitis: chronic low-grade inflammation.

### Limitations

There are several limitations of this review. Studies included were cross-sectional or case-control in nature. Since all the included studies were of level IV evidence, no further risk of bias assessment was done.

Prospective studies are needed in the future for better quality evidence on this topic. Meta-analysis could not be carried out due to marked heterogeneity between the studies. Definition of periodontitis and cutoff values of CAL varied across studies. The studies included in the review were not homogenous with regard to the use of anti-resorptive therapy, with some studies excluding patients taking such treatment.

A strong association between CAL and osteoporosis was confirmed. Further community-based studies prospective are required to justify the strength of this association. More information is needed on improvement of CAL and other clinical and laboratory markers of chronic periodontitis with improvement of BMD with medical treatment with antiresorptive agents. This may be difficult as any significant improvement in BMD with treatment will need several years of follow-up.

### CONCLUSION

Chronic periodontitis is strongly associated with osteoporosis in postmenopausal women.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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