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Association of testosterone and bone mineral density with tooth loss in men with chronic periodontitis

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Abstract: A study was conducted to compare the mean testosterone and bone mineral density (BMD) levels in men with and without tooth loss. Two hundred three male subjects aged 30-65 years satisfying the study criteria were selected and then examined for bone mineral density, testosterone level, clinical attachment loss, probing pocket depth, tooth mobility and tooth loss due to periodontal disease. Statistical analysis was performed using the Statistical Package for Social Sciences (version 15.0) (SPSS Inc., Chicago, Ill, USA), and differences were considered to be significant at $P < 0.05$. Independent sample "*t*" test was used to compare the results, and receiver-operator curve (ROC) analysis was performed to obtain the cut-off. The mean testosterone level in subjects without tooth loss was 4.41 ± 2.57, whereas that in subjects with tooth loss was 2.79 ± 1.15 ($P = 0.001$). The mean BMD in subjects without tooth loss was 0.99 ± 0.13, whereas that in subjects with tooth loss was 0.96 ± 0.12 ($P = 0.046$). The testosterone level and BMD in subjects with tooth loss were significantly lower than those in subjects without tooth loss. Testosterone is a good predictor of tooth loss, but its efficiency decreases with increasing tooth loss. BMD is not a good predictor of tooth loss. (J Oral Sci 53, 333-339, 2011)

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Introduction

Since alveolar bone loss is a prominent feature of periodontal disease, disturbances of bone metabolism (due to hormonal changes) and a decrease of skeletal bone mineral density, especially in the jaws, are suspected to be aggravating factors of periodontal disease (1-3). This alveolar bone loss associated with chronic periodontitis leads to tooth loss.

Testosterone plays an important role in the regulation of bone turnover and bone mass in men (4) by promoting bone formation (5). A decreased testosterone level leads to an increase of alveolar bone loss and an altered trabecular pattern (in the presence of periodontitis) (6), as well as a decrease in the bone mineral density of skeletal tissue, including the maxilla and mandible (7). Therefore, it has been hypothesized that a decrease in the level of testosterone with an associated reduction of bone mineral density in the presence of periodontitis can lead to tooth loss. However, this relationship is difficult to establish, as the results may easily be confounded by other factors such as gender, hormone intake, smoking, race and age (8,9).

A few studies have documented the relationship of tooth loss with bone mineral density and testosterone (10-12), but the results have differed due to insufficiency of sample size, non-comparability of the selected subjects, and differences in the methods used for measuring bone

mineral density. Accordingly, this relationship has remained unclear.

The present study was planned to compare the mean testosterone level and bone mineral density in male subjects with and without tooth loss in the presence of moderate periodontitis. An attempt was also made to find a testosterone level cut-off point and the mean BMD that would allow prediction of tooth loss with satisfactory efficiency.

Materials and Methods

A total of 500 male patients aged between 45 and 65 years attending the outpatient department of Prosthodontics from Chhatrapati Shahuji Maharaj (CSM) Medical University, Lucknow, were screened, among whom 203 who fulfilled the selection criteria participated in the present study. The protocol was approved by the institutional ethics committee and written informed consent was obtained from the participants. Subjects were included in the study after obtaining their medical histories and undergoing a clinical examination. All the subjects had generalized moderate chronic periodontitis, with or without tooth loss. Subjects with a history of, or treatment for, endocrine, metabolic or skeletal diseases, smoking or alcohol intake, or any drug regimen that could affect the periodontium in any way were excluded from the study.

The periodontal assessment of the study participants was conducted by a single examiner (VG), and the parameters included were clinical attachment loss (CAL), probing pocket depth (PPD), and mobility. CAL and PPD were measured at four sites per tooth. Subjects with CAL of 3-4 mm at ≥30% of the examined sites were classified as having generalized moderate chronic periodontitis, and only these subjects were included in the study. Partially dentate patients with a history of tooth loss/extraction for periodontal reasons were strictly selected. A final total of 203 otherwise systemically healthy men with either complete or partial dentition and suffering from generalized moderate chronic periodontitis were selected for our study. The subjects were sorted into three groups on the basis of different tooth loss criteria:

Group 1: Completely dentate and partially dentate
Group 2: Tooth loss ≤3 and >3
Group 3: Tooth loss ≤5 and >5

The serum testosterone level was determined by enzyme immunoassay by one of the authors (AM) using a commercially available kit (DRG Instruments GmbH, Marburg, Germany) in accordance with the manufacturer's instructions (13).

BMD expressed as T-score was measured using dual-energy X-ray absorptiometry (DEXA) with a fanbeam bone densitometer (GE-Lunar Prodigy, Madison, WI, USA) at the forearm, lumbar spine (L1-L4) and total hip (14,15), and the mean BMD was calculated for each subject.

The observations were performed by the investigator and the co-investigator, both simultaneously and independently, so that they were unable to see the scores assigned. Thereafter the scores were compared using paired *t* test, and no significant difference ($P > 0.05$) was found. The average of the scores assigned by the two different observers was used for the study. Statistical analysis was performed using the Statistical Package for the Social Sciences (version 15.0, SPSS Inc., Chicago, IL, USA). The significance of differences was assessed using analysis of variance (ANOVA). Different parameters were assessed using Pearson's correlation coefficient. Differences were considered to be significant at $P < 0.05$. Independent sample "*t*" test was used to compare the mean testosterone levels and mean BMD between subjects who had tooth loss and those who did not. Bivariate correlation was used to clarify the relationship between testosterone levels and BMD. Receiver-operator curve (ROC) analysis was performed to obtain the cut-off point for the testosterone level and mean BMD that would predict tooth loss with satisfactory efficiency.

Table 1 Testing an association between testosterone and level of tooth loss

No.	Group	Comparison						Significance of difference	
		No tooth loss (n = 105)			With tooth loss (n = 98)				
		Mean	SD	SEM	Mean	SD	SEM	"*t*"	"*P*"
1	Group I	4.41	2.57	0.25	2.79	1.15	0.12	5.715	<0.001
		Tooth loss ≤3 (n = 163)			Tooth loss >3 (n = 40)				
2	Group II	3.88	2.28	0.18	2.59	1.20	0.19	3.467	0.001
		Tooth loss ≤5 (n = 174)			Tooth loss >5 (n = 29)				
3	Group III	3.79	2.25	0.17	2.62	1.26	0.23	2.378	0.007

Results

The mean testosterone level in subjects without tooth loss was 4.41 ± 2.57, whereas it was 2.79 ± 1.15 for subjects with tooth loss. The difference between the groups was statistically significant (Table 1). The area under the curve was 0.767, which was also statistically significant ($P < 0.001$). A cut-off of ≤3.007 was found to be 63.3% sensitive and 79% specific, whereas a cut-off of ≤3.281 was 71.4% sensitive and 74.3% specific (Fig. 1).

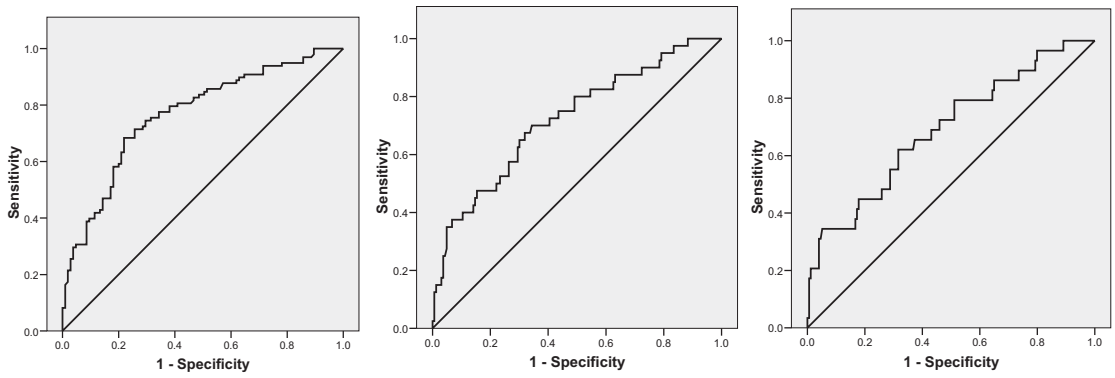
The mean testosterone level in subjects with ≤3 tooth loss was 3.88 ± 2.28, whereas it was 2.59 ± 1.20 in subjects with >3 tooth loss. The difference between the groups was statistically significant (Table 1). The area under the curve was 0.721, which was also statistically significant ($P < 0.001$). A cut-off of ≤3.07 indicated a sensitivity of 70% and a specificity of 65.6% (Fig. 1).

The mean testosterone level in subjects with ≤5 tooth loss was 3.79 ± 2.25, whereas it was 2.62 ± 1.26 in subjects with >5 tooth loss. The difference between the groups was statistically significant (Table 1). The area under curve was 0.691, which was also statistically significant ($P < 0.001$). A cut-off of ≤3.07 indicated a sensitivity of 65.5% and a specificity of 62.6% (Fig. 1).

The mean BMD in subjects without tooth loss was 0.99 ± 0.13, whereas it was 0.96 ± 0.12 in subjects with tooth loss. The difference between the groups was statistically significant (Table 2). In a normal distribution with a large sample size, the difference was significant for small differences too. The area under the curve was found to be 0.565, which was too close to the null hypothesis true area = 0.5. The optimum cut-off value was ≤0.961, which gave a sensitivity of 55.1% and a specificity of 54.3%, which did not have good predictive value (Fig. 2).

The mean BMD in subjects with ≤3 tooth loss was 0.98 ± 0.13, whereas it was 0.94 ± 0.13 in subjects with >3 tooth loss. The difference between the groups was statistically significant (Table 2). The area under the curve was 0.594, which was too close to the null hypothesis true area = 0.5. The optimum cut-off value was ≤0.9565, yielding a sensitivity of 60% and a specificity of 57.4%, which was not found to have good predictive value (Fig. 2).

The mean BMD in subjects with ≤5 tooth loss was 0.98 ± 0.13, whereas it was 0.92 ± 0.12 in subjects with



(a) Group I (b) Group II (c) Group III

Area under the curve
Test result variable(s): Testosterone

Group I = No tooth loss vs Tooth loss				
			Asymptotic 95% Confidence Interval	
Area	Std. Error (a)	Asymptotic Sig. (b)	Lower	Upper
0.767	0.033	0.000	0.701	0.832
Group II = Teeth loss ≤3 teeth vs >3 teeth				
			Asymptotic 95% Confidence Interval	
Area	Std. Error (a)	Asymptotic Sig. (b)	Lower	Upper
0.721	0.046	<0.001	0.630	0.812
Group III = Teeth loss ≤5 teeth vs >5 teeth				
			Asymptotic 95% Confidence Interval	
Area	Std. Error (a)	Asymptotic Sig. (b)	Lower	Upper
0.691	0.055	0.001	0.583	0.798

The test result variable(s): Testosterone has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.
a Under the nonparametric assumption
b Null hypothesis: true area = 0.5

Fig. 1 Calculation of a cut-off point of testosterone level to predict tooth loss.

>5 tooth loss. The difference between the groups was statistically significant (Table 2). The area under the curve was 0.633, which was also statistically significant (P = 0.022). The optimum cut-off value was ≤0.9565, which yielded a sensitivity of 65.5% and a specificity of 66.3%, which was reasonably predictive (Fig. 2).

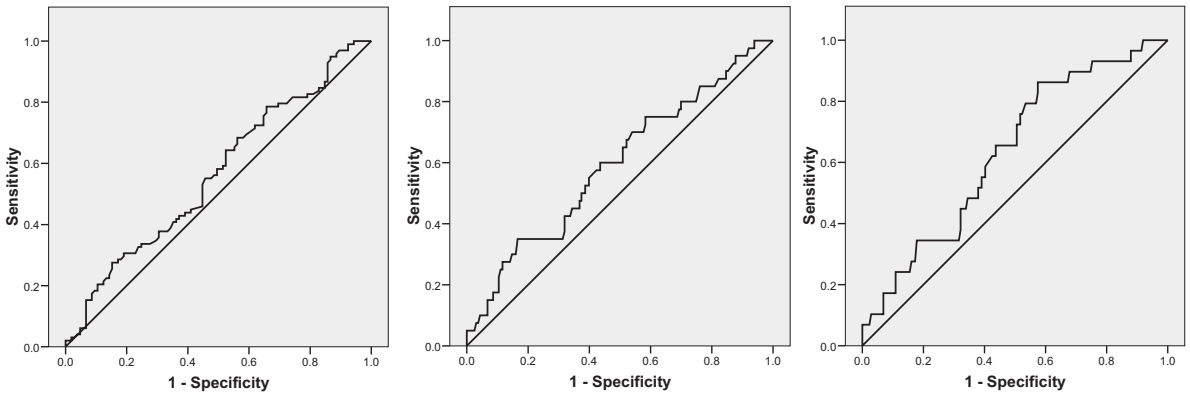
The calculated Pearson bivariate correlation coefficient was +0.082, which was almost negligible (no association between testosterone and bone mineral density) (Fig. 3).

Discussion

Periodontal disease represents a group of bacterial infections and inflammatory diseases that result in the destruction of tooth-supporting tissue, including the gingiva, alveolar bone and the teeth themselves, eventually causing tooth loss (16). The role of testosterone and bone mineral density in the progression of periodontal disease has not been well documented. Some studies have suggested that these conditions may cause changes in alveolar bone, such as increased alveolar porosity, an

Table 2 Testing an association between BMD and level of tooth loss

No.	Group	Comparison						Significance of difference	
		No tooth loss (n = 105)			With tooth loss (n = 98)				
		Mean	SD	SEM	Mean	SD	SEM	"t"	"P"
1	Group I	0.9920	0.13276	.01296	0.9557	0.12374	.01250	2.008	0.046
		Tooth loss ≤3 (n = 163)			Tooth loss >3 (n = 40)				
2	Group II	0.9840	0.12810	0.01003	0.9358	0.12928	0.02044	2.129	0.034
		Tooth loss ≤5 (n = 174)			Tooth loss >5 (n = 29)				
3	Group III	0.9839	0.129	0.010	0.9179	0.117	0.217	2.577	0.011



(a) Group I (b) Group II (c) Group III

Area under the Curve
Test Result Variable(s): BMD

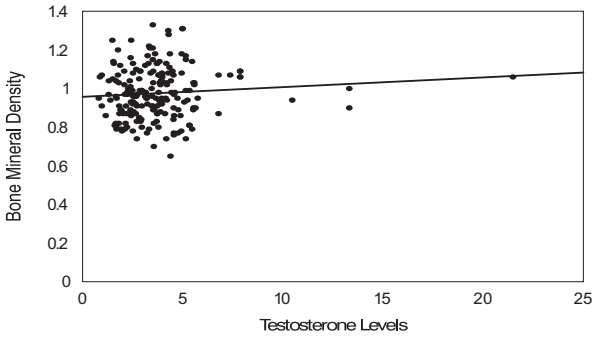
Area	Std. Error (a)	Asymptotic Sig. (b)	Asymptotic 95% Confidence Interval Lower	Upper
Group I = No tooth loss vs Tooth loss				
0.565	0.040	0.108	0.486	0.644
Group II = Teeth loss ≤3 teeth vs >3 teeth				
0.594	0.051	0.066	0.494	0.693
Group III = Teeth loss ≤5 teeth vs >5 teeth				
0.633	0.052	0.022	0.531	0.735

The test result variable(s): BMD has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.
a Under the nonparametric assumption
b Null hypothesis: true area = 0.5

Fig.2 Calculation of a cut-off point of BMD levels to predict tooth loss.

altered trabecular pattern, rapid alveolar bone resorption and modification of the local tissue response by increasing the systemic release of interleukin-1 and interleukin-6 following invasion by periodontal pathogens (6,17,18).

The prevalence, magnitude and severity of periodontitis are high in India. The proportion of the population affected increases with age, and reaches 95-100% in the later part of life, i.e. the fifth and sixth decades (19). Periodontitis is the second most common cause of tooth loss in males (20). Therefore the present study was planned to clarify the levels of testosterone and bone mineral density in men with and without tooth loss. To standardize the study, we chose subjects who were attending our outpatient department because of chronic moderate periodontitis.



r = 0.082; $P = 0.246$

Fig.3 Association between BMD and testosterone levels.

The level of testosterone in subjects with tooth loss was found to be significantly lower than in those without tooth loss. Testosterone is known to affect bone metabolism by influencing existing periodontitis through modulation of immunological events (10,11). Furthermore, it has been reported that a decrease of testosterone is compensated by a relative excess of catabolic hormones (cortisone and hydrocortisone); this causes bone resorption to take place faster than bone formation, resulting in reduction of bone mass, which can lead to tooth loss (21). ROC analysis was able to calculate a cut-off point with reasonable sensitivity and specificity, suggesting that the level of testosterone is a good predictor of tooth loss.

It was found that testosterone levels in subjects with higher tooth loss (>3 or >5) were significantly lower than in those without ($P = 0.001$ and $P = 0.007$). A cut-off of ≤3.07 indicated a sensitivity of 70% and a specificity of 65.6% (Fig. 1), which meant that the ROC was able to calculate the cut-off point with reasonable sensitivity

Table 3 Multivariate analysis to know the number of tooth loss as a function of testosterone levels and BMD

Coefficients (a)

Model		Unstandardized Coefficients		Standardized Coefficients	T	Sig.
		B	Std. Error	Beta	B	Std. Error
1	(Constant)	11.288	3.079		3.666	0.000
	Testosterone	-0.568	0.186	-0.209	-3.058	0.003
	BMD	-6.513	3.113	-0.143	-2.092	0.038

Dependent variable: Tooth loss

Generated equation: $y = a + b_1x_1 + b_2x_2$

Where y = number of tooth lost; a is a constant, b_1 and b_2 are coefficients for the independent variables testosterone and BMD respectively.

y = 11.288 – (0.568*Testosterone levels) – (6.513*BMD levels)

Table 4 Number of tooth loss as a function of testosterone levels and BMD (only subjects with tooth loss included)

Coefficients (a, b)

Model		Unstandardized Coefficients		Standardized Coefficients	T	Sig.
		B	Std. Error	Beta	B	Std. Error
1	(Constant)	16.586	6.028		2.751	0.007
	Testosterone	-0.628	0.639	-0.099	-0.983	0.328
	BMD	-9.277	5.963	-0.157	-1.556	0.123

Dependent variable: Tooth loss

After taking only the subjects with tooth loss the modified equation becomes:

y = 16.586 – (0.628*Testosterone levels) – (9.277*BMD levels)

But here none of the independent variables has got a significant association with the outcome hence it is liable to be rejected.

and specificity. A cut-off of ≤3.07 yielded a sensitivity of 65.5% and a specificity of 62.6%, which meant that the ROC was able to calculate a cut-off point with workable sensitivity and specificity (Fig. 1). Thus, testosterone was found to lose its efficiency as an indicator with increasing tooth loss.

A decrease in bone mineral density also causes alveolar bone loss, as well as modifying the local tissue response to periodontitis, leading to reduction of clinical attachment, and tooth loss (18,22,23). It has been reported that the BMD of skeletal tissue may be used as an indicator of the BMD of the maxilla and mandible. Maxillary and mandibular BMD is difficult to measure accurately because of superimposition of the tooth portion, and varying technical sensitivity (24). Therefore, it was hypothesized that the BMD of subjects with tooth loss would be significantly lower than in those without tooth loss. Table 2 shows that the BMD of subjects with tooth loss was, in fact, significantly lower than that of subjects without tooth loss, thus confirming the hypothesis. An optimum cut-off value was obtained at ≤0.961, and this yielded a sensitivity of 55.1% and a specificity of 54.3%, which did not provide good predictive value. The ROC was unable to provide an optimum cut-off point for a reasonable predictive value. The BMD of subjects with higher tooth loss (>3 or >5) was found to be significantly lower than that of subjects without any tooth loss (P = 0.034 and P = 0.011 respectively). The ROC was unable to yield an optimum cut-off point for a reasonable predictive value for >3 tooth loss, but was able to do so for an optimum cut-off point that was reasonably predictive for >5 tooth loss. This suggests that BMD is not a good predictor of tooth loss, but is a good predictor of higher tooth loss (>5).

No correlation was seen between BMD and testosterone level (P = +0.082). Thus a combination of BMD and testosterone level might have some impact for prediction of tooth loss.

The number of teeth lost was considered to be a function of testosterone level and BMD. Therefore, multivariate analysis was performed using a linear regression method (Table 3), and the equation generated was:

Y = 11.288 – (0.568* testosterone level) – (6.513* BMD level)

The outcome showed that in a model where the number of missing teeth was a factor dependent on testosterone and BMD as independent variables, both of the independent variables had a significant association with outcome.

The number of missing teeth was considered to be a function of testosterone level and BMD (only subject with tooth loss being included). Linear regression (Table 4) after taking only the subjects with tooth loss modified the equation to:

Y = 16.586 – (0.628* testosterone level) – (9.277* BMD level)

Here, none of the independent variables showed a significant association with outcome, and thus the null hypothesis was rejected. Thus it was shown that a combination of testosterone level and BMD is more efficient for predicting the event of tooth loss rather than the number of teeth lost.

Since the subjects selected had generalized moderate chronic periodontitis, the results are representative of existing periodontitis in subjects with low BMD in whom the level of testosterone modifies the progression of periodontitis, thus contributing to tooth loss.

The present study had certain limitations. First, it was based on the patient's version of the cause of tooth loss. Furthermore, there are no reports that would allow comparison of data for Indian males living in other parts of the country.

Testosterone is a good predictor of tooth loss but loses its efficiency with increasing tooth loss. Bone mineral density is not a good predictor of tooth loss (<5) but is predictive of higher tooth loss (>5). A combination of BMD and testosterone level might have more impact for prediction of tooth loss.

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