Original Article

Correlation of Mandibular Radiomorphometric Indices with Serum Calcium and Serum Estradiol in Pre- and Post-menopausal Women

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Abstract

Background: Osteoporosis is a disease that is seen commonly with increasing age. The purpose of this study was to compare the bone quality of pre- and post-menopausal women using the quantitative indices determined by measurements on panoramic radiographs (mental index, inferior and superior panoramic mandibular indices, antegonion index [AGI], and gonion index) and to determine the effects of serum calcium and serum estradiol levels on alveolar bone loss. **Materials and Methods:** Sixty female patients in the age group of 25–55 years were included in the study. The patients were divided into three equal groups, i.e., control Group A (twenty - premenopausal women), study Group B (twenty - postmenopausal women with healthy periodontium), study Group C (twenty - postmenopausal women with periodontitis). Quantitative indices were measured on digital panoramic radiographs of the patients and serum calcium and estradiol levels were determined. **Results:** Correlation of serum calcium with radiomorphometric indices of all the groups showed statistically nonsignificant differences. On correlating mean estradiol levels with radiographic indices of patients of Group A and Group B showed statistically nonsignificant differences. On correlating mean estradiol levels with radiographic indices of patients of Group C patients showed statistically significant difference with positive correlation with cortical width (P = 0.04) and AGI (P = 0.02) while statistically nonsignificant correlation with other indices. The statistical tests used for the analysis of the result were one-way ANOVA, multiple comparison Tukey test, Chi-square test, Student's t-test. **Conclusion:** There is a little evidence of correlation of these indices with serum estradiol and calcium levels, and therefore, detailed further research about this correlation is required.

Keywords: *Osteoporosis, periodontitis, radiomorphometric indices, serum calcium, serum estradiol*

Introduction

Skeletal osteopenia diagnosed from plain radiographs of the hip or lumbar spine is recognized as an indication for bone densitometry. Analogously dentists may recognize patients with low bone mineral density (BMD) by evidence of mandibular osteopenia and refer such patients to undergo BMD assessment using dual X-ray energy absorptiometry (DXA).[1]

Falling concentrations of estrogen at the menopause are associated with low bone density.[2] Changes occurring at menopause have also shown to affect the levels of serum calcium.[3] Hence, the purpose of this study was to compare the bone quality of pre- and post-menopausal women using the quantitative indices and to correlate them with levels of serum calcium and serum estradiol.

Materials and Methods

After obtaining permission from the Institutional Ethics Committee, this study was conducted in the Department of Oral Medicine and Radiology, patients were briefed regarding the study, and prior written consent from patient was taken. Total sixty female patients in the age group of 25–55 years were included in the study from the patients attending the outpatient Department of Oral Medicine and Radiology. The patients were divided into three equal groups as follows:

Group A - control Group A (twenty - premenopausal women with healthy periodontium). Group B - study Group B (twenty - postmenopausal women with healthy periodontium). Group C - study Group C (twenty - postmenopausal women suffering from periodontitis).

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All the patients were screened by taking the detailed menstrual history (including years since menopause). Clinical attachment loss (CAL) was measured using William's periodontal probe. The attachment levels were stratified into CAL ≤3 mm (absence of periodontitis or mild periodontitis), >3–≤6 (defined as moderate periodontitis), and CAL >6 mm (defined as severe periodontitis). Digital panoramic radiographs were taken for all the patients using the same Orthopantomograph machine Planmeca Proline EC.

Inclusion criteria

- Premenopausal women in good general health, not suffering from any systemic disorder or condition
- Postmenopausal women within 10 years of menopause
- Postmenopausal women suffering from moderate chronic periodontitis (3–4 mm of CAL) or severe chronic periodontitis (>5 mm CAL) with good oral hygiene.

Exclusion criteria

- Patients taking estrogen, corticosteroids, or any other therapy or suffering from parathyroid dysfunction
- Paget's disease or any other disorder likely to affect calcium metabolism such as renal dysfunction
- Patients on drugs that can cause increased measurements in calcium levels including calcium salts (e.g., nutritional supplements or antacids), Vitamin D, lithium, thiazide diuretics, and thyroxine
- Tobacco users.

Method for estimation of quantitative mandibular indices

Dental digital panoramic radiograph of each patient was taken with the same X-ray machine (Planmeca PM 2002 CC Proline, Helsinki, Finland) at 12 mA, 15 s, and 70–80 kv. The films were processed by an automated X-ray film processor.

Panoramic mandibular index

Panoramic mandibular index (PMI) is a radiomorphometric index introduced in 1991 by Benson *et al*. It was defined as the ratio of the thickness of the inferior mandibular cortex in the mental region over the distance between inferior and/or superior border of the mental foramen. Three measurements comprising mandibular index and PMI were carried out both for the left and right sides using the following technique [Figure 1] and using the measure tool of the software:

1. The mental foramina was identified
2. A line (b) was drawn which passed perpendicular to the tangent to the lower border of the mandible (a) and through the center of the mental foramina
3. Measurements were made along this line of:
    - Cortical width (c)
    - The distance between the lower border of the mandible and the inferior margin of the mental foramina (inferior foraminal distance, I)
    - The distance between the lower border of the mandible and the superior margin of the mental foramina (superior foraminal distance, S).

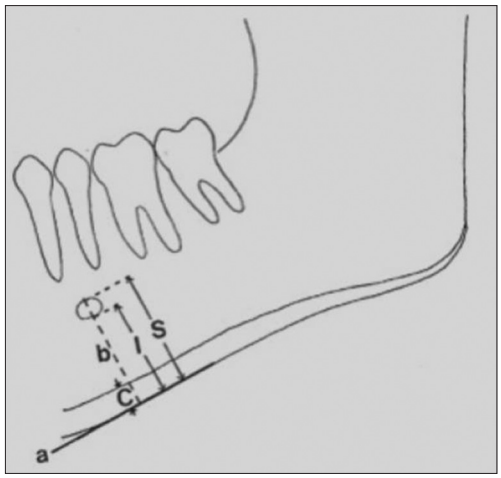


Figure 1: Measurement for superior panoramic mandibular index and inferior panoramic mandibular index

Superior and inferior PMI (IPMI) were calculated as:

- Superior PMI (SPMI) = cortical thickness(C)/distance from superior margin of mental foramen to inferior border of mandible(S)
- IPMI = cortical thickness(C)/distance from inferior margin of mental foramen to inferior border of mandible(I)
- When the superior border of the mandibular cortex was ill defined on the radiographs, the smallest width of compact cortical bone lying above the mental foramen was measured.

Mental index or cortical width or mean cortical thickness

Mental index is defined as the cortical width (C) below the mental foramina [Figure 1].

Antegonion index

The antegonion index (AGI) is a measurement of cortical width in the region anterior to the gonion at a point identified by extending a line of best fit on the anterior border of the ascending ramus down to the lower border of the mandible. Where the anterior border of the ramus was markedly curved, the line was drawn as closely as possible to the straighter, inferior, part of the bone margin above the third molar region [Figure 2].

Gonion index

Gonion index (GI) was measured according to the method of Bras *et al*. Thickness of the mandibular angular cortex on the panoramic radiographs was measured. To determine the location of the gonion, a vertical tangent to the posterior border of ramus was drawn. The angle made by this line

with the tangent to the lower border of mandible at mental foramen was bisected. At a point of intersection of this bisector line with the angle of mandible, the thickness of angular cortex was measured [Figure 3].

For the particular index, the index score for a patient was determined by calculating the average of the right and left side scores of that index.

The patient was asked to sit comfortably on dental chair, after applying the tourniquet in arm and cleaning the antecubital fossa with cotton swab soaked in 70% alcohol, 5 ml of blood was withdrawn from cubital vein with 24 gauge needle. 4.5 ml of blood was then transferred to plain sterile bulb which was kept undisturbed for half an hour at room temperature. The supernatant was removed and centrifuged at 3000 rpm for 4–5 min. The serum was taken to the laboratory for estimation of serum estradiol and serum calcium level. Samples were stored at −20°C.

Method for serum estradiol II estimation

Serum estradiol II was estimated by Vidas method, an automated quantitative estimation of serum estradiol, using Vidas estradiol kit (Biomerieux kit).

Method for serum calcium estimation

Serum calcium was estimated by modified Arsenazo method (Pathozyme kit) and instrument used was ultraviolet-visible spectrophotometer (ELICO SL - 244).

Statistical analysis

Statistical analysis for the correlation of calcium and estradiol levels with radiographic indices of each group was carried out. All the variables from the study were analyzed for the mean values, standard deviation, standard error, range, and "*P*" value to find the significant difference between those values. The statistical tests used for the analysis of the result were one-way ANOVA, multiple comparison Tukey test, Chi-square test, and Student's *t*-test.

In all the above tests, $P < 0.05$ was taken to be statistically significant; $P > 0.05$ was taken to be statistically nonsignificant.

Observations and Results

Tables 1-6 showing the mean values of serum calcium, serum estradiol, and mean values of the mandibular radiomorphometric indices of the three groups (Groups A, B, and C), respectively.

On correlating levels of mean serum calcium of patients of Groups A, B, and C (control group) with mean cortical width, mean SPMI, mean IPMI, mean AGI, and mean GI, respectively, showed statistically nonsignificant differences ($P > 0.05$) [Tables 1, 3 and 5]. Furthermore, on correlating levels of mean serum estradiol of patients of Group A and B with mean cortical width, mean SPMI, mean IPMI, mean AGI, and mean GI showed statistically nonsignificant differences ($P > 0.05$) [Tables 2 and 4].

Table 1: Correlation of mean serum calcium level (mg/dl) with mean - mental index (mm), superior panoramic mandibular index, inferior panoramic mandibular index, antegonion index (mm), and gonion index (mm) in Group A

Clinical parameters	Mean±SD	*n*	Correlation "*r*"	*P*
Serum calcium (mg/dl)	10.98±1.22	20	-	-
Cortical width (MI) (mm)	4.39±0.74	20	0.24	0.29, NS, >0.05
SPMI	0.28±0.04	20	0.14	0.54, NS, >0.05
IPMI	0.34±0.06	20	0.11	0.63, NS, >0.05
AGI (mm)	3.07±0.59	20	0.25	0.27, NS, >0.05
GI (mm)	1.55±0.30	20	0.30	0.18, NS, >0.05

MI: Mental index; SPMI: Superior panoramic mandibular index; IPMI: Inferior panoramic mandibular index; AGI: Antegonion index; GI: Gonion index, NS: Not significant, SD: Standard deviation

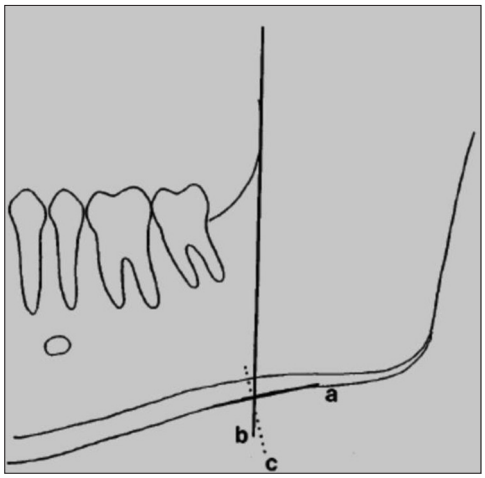


Figure 2: Measurement for cortical width mental index

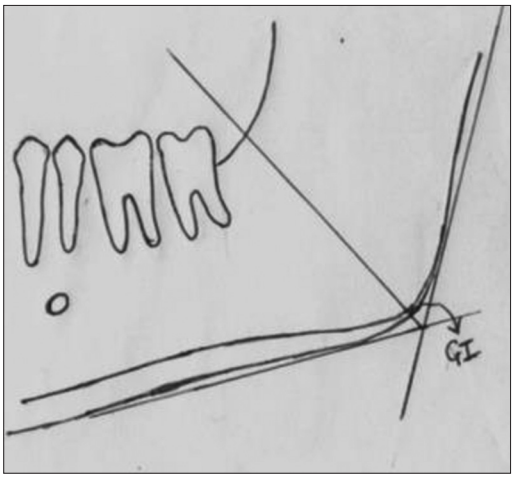


Figure 3: Measurement for gonion index

Table 2: Correlation of mean serum estradiol level (pg/ml) with mean - mental index (mm), superior panoramic mandibular index, inferior panoramic mandibular index, antegonion index (mm), and gonion index (mm) in Group A

Clinical parameters	Mean±SD	*n*	Correlation "*r*"	*P*
Serum estradiol (pg/ml)	324.91±304.15	20	-	-
Cortical width (MI) (mm)	4.39±0.74	20	0.05	0.80, NS, >0.05
SPMI	0.28±0.04	20	−0.06	0.77, NS, >0.05
IPMI	0.34±0.06	20	0.04	0.84, NS, >0.05
AGI (mm)	3.07±0.59	20	−0.08	0.71, NS, >0.05
GI (mm)	1.55±0.30	20	0.11	0.64, NS, >0.05

MI: Mental index; SPMI: Superior panoramic mandibular index; IPMI: Inferior panoramic mandibular index; AGI: Antegonion index; GI: Gonion index, NS: Not significant, SD: Standard deviation

Table 3: Correlation of mean serum calcium level (mg/dl) with mean - mental index (mm), superior panoramic mandibular index, inferior panoramic mandibular index, antegonion index (mm), and gonion index (mm) in Group B

Clinical parameters	Mean±SD	*n*	Correlation "*r*"	*P*
Serum calcium (mg/dl)	10.99±1.42	20	-	-
Cortical width (MI) (mm)	4.10±0.87	20	0.32	0.156, NS, >0.05
SPMI	0.25±0.06	20	0.07	0.740, NS, >0.05
IPMI	0.29±0.07	20	0.04	0.843, NS, >0.05
AGI (mm)	2.85±0.41	20	−0.08	0.710, NS, >0.05
GI (mm)	1.330±0.21	20	0.25	0.285, NS, >0.05

MI: Mental index; SPMI: Superior panoramic mandibular index; IPMI: Inferior panoramic mandibular index; AGI: Antegonion index; GI: Gonion index, NS: Not significant, SD: Standard deviation

Table 4: Correlation of mean serum estradiol level (pg/ml) with mean - mental index (mm), superior panoramic mandibular index, inferior panoramic mandibular index, antegonion index, (mm) and gonion index (mm) in Group B

Clinical parameters	Mean±SD	*n*	Correlation "*r*"	*P*
Serum estradiol (pg/ml)	89.97±205.27	20	-	-
Cortical width (MI) (mm)	4.10±0.87	20	0.01	0.96, NS, >0.05
SPMI	0.25±0.06	20	0.16	0.49, NS, >0.05
IPMI	0.29±0.07	20	0.20	0.37, NS, >0.05
AGI (mm)	2.85±0.41	20	0.19	0.40, NS, >0.05
GI (mm)	1.330±0.21	20	−0.33	0.15, NS, >0.05

MI: Mental index; SPMI: Superior panoramic mandibular index; IPMI: Inferior panoramic mandibular index; AGI: Antegonion index; GI: Gonion index, NS: Not significant, SD: Standard deviation

Table 5: Correlation of mean serum calcium level (mg/dl) with mean - mental index (mm), superior panoramic mandibular index, inferior panoramic mandibular index, antegonion index (mm), and gonion index (mm) in Group C

Clinical parameters	Mean±SD	*n*	Correlation "*r*"	*P*
Serum calcium (mg/dl)	10.25±1.02	20	-	-
Cortical width (MI) (mm)	3.42±0.68	20	−0.12	0.60, NS, >0.05
SPMI	0.22±0.04	20	−0.11	0.63, NS, >0.05
IPMI	0.27±0.05	20	−0.15	0.52, NS, >0.05
AGI (mm)	2.72±0.53	20	−0.05	0.80, NS, >0.05
GI (mm)	1.21±0.30	20	0.05	0.83, NS, >0.05

MI: Mental index; SPMI: Superior panoramic mandibular index; IPMI: Inferior panoramic mandibular index; AGI: Antegonion index; GI: Gonion index, NS: Not significant, SD: Standard deviation

Whereas on correlating levels of mean serum estradiol of patients of Group C (study group) with mean cortical width, mean SPMI, mean IPMI, mean AGI, and mean GI, respectively, showed statistically significant difference with positive correlation with cortical width ($P = 0.04$) and AGI ($P = 0.02$) while statistically nonsignificant correlation with SPMI, IPMI, and GI [Table 6 and Graphs 1, 2].

Discussion

The dental radiographs are regularly made on a large fraction of the adult population which can make their potential use as a marker of skeletal health and an exciting avenue of research. In practice, this means deciding who is a candidate for DEXA testing. Unfortunately, there is no known combination of risk factors that are both sensitive and specific for identifying individuals likely to have osteoporosis. The goal of such screening is not to diagnose osteoporosis but rather to identify individuals at risk of having osteoporosis and refer them appropriately.[4]

Due to economy and affordability concerns, we opted to use radiographic indices and serum values of calcium and estradiol for provisional screening of postmenopausal women and to provide people within rural setup with an easy facility of assessing osteoporotic changes and then refer them for BMD assessment by DXA scan if required.

There is a decrease in BMD of women in the postmenopause, more within 3 years of menopause and estradiol levels correlating positively with BMD.[5] Hence, we considered patients in Group A premenopausal women with healthy nonosteoporotic changes and patients in Group B and Group C postmenopausal women with decreased levels of estradiol and at increased risk of osteoporotic changes.

Almost all of the body's calcium are stored in the skeleton and it is an essential nutrient for bone. It has been concluded that calcium supplementation is a cornerstone of any treatment regimen for osteoporosis.[6]

The results of the present study were similar to those of Okyay *et al*. who found no significant differences in calcium levels in women with and without osteoporosis.[6] The results of the present study were unlike those obtained by Ramesh *et al*. in whose study the mean serum calcium in premenopausal women was 9.2 ± 0.46 mg/dl, postmenopausal women with healthy periodontium had mean serum calcium 8.64 ± 0.30 mg/dl, and 7.01 ± 0.46 mg/dl in postmenopausal women with periodontitis with statistically significant differences between and among the three groups.[3]

Table 6: Correlation of mean serum estradiol level (pg/ml) with mean - mental index (mm), superior panoramic mandibular index, inferior panoramic mandibular index, antegonion index (mm), and gonion index (mm) in Group C

Clinical parameters	Mean±SD	*n*	Correlation "*r*"	*P*
Serum estradiol (pg/ml)	43.46±65.75	20	-	-
Cortical width (MI) (mm)	3.42±0.68	20	0.45	0.04, S, <0.05
SPMI	0.22±0.04	20	0.19	0.42, NS, >0.05
IPMI	0.27±0.05	20	0.16	0.49, NS, >0.05
AGI (mm)	2.72±0.53	20	0.48	0.02, S, <0.05
GI (mm)	1.21±0.30	20	0.27	0.23, NS, >0.05

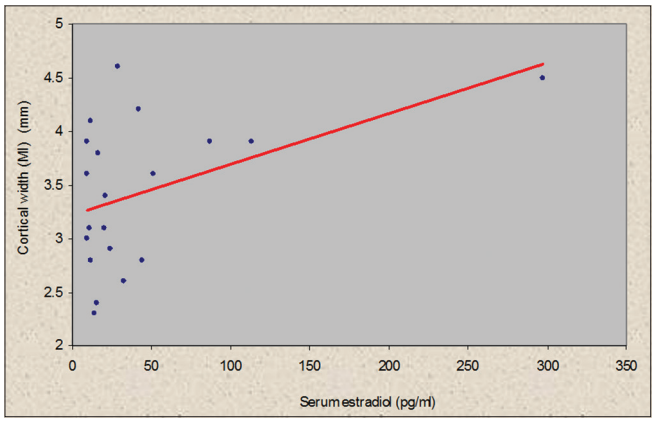
MI: Mental index; SPMI: Superior panoramic mandibular index; IPMI: Inferior panoramic mandibular index; AGI: Antegonion index; GI: Gonion index, NS: Not significant, S: Significant, SD: Standard deviation

The results of the present study were similar to the study by Ramesh *et al*.; in their study, they correlated the levels of mean serum calcium with PMI in pre- and post-menopausal women and did not find any statistically significant correlation.[3]

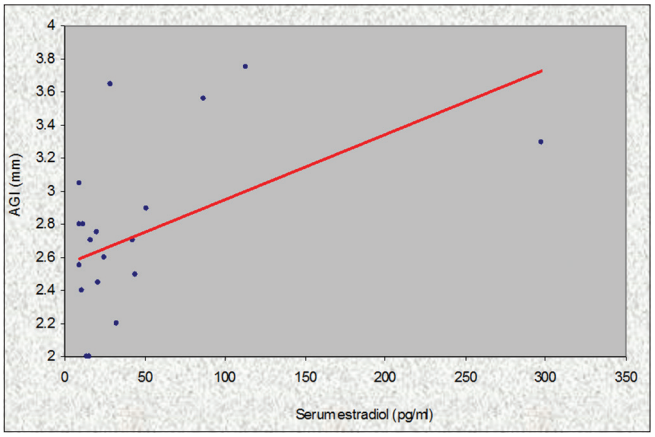
During the menopausal transition, ovarian production of estrogen and progesterone declines. This natural endocrine transition is associated with diminished circulating levels of estradiol (E2).[7] Menopause-related estrogen withdrawal might contribute to make bone more vulnerable to oxidative injury thereby increasing the risk of postmenopausal osteoporosis development.[8] Postmenopausal bone loss follows a pattern with an early estrogen-dependent phase of rapid decline in bone mass followed by an age-related bone loss at a constant, slower rate throughout aging.[9] Bone loss in postmenopausal women is mainly due to estrogen deficiency affecting the balance between osteoclast resorption and bone formation controlled by osteoblasts.[10]

The results of the present study were similar to those by Reddy Kilim and Chandala, in their study, the mean estradiol levels in premenopausal women was 175.48 ± 43.20 pg/ml and mean level in postmenopausal women was 44.18 ± 10.52 pg/ml with statistically significant differences between the levels of the two groups; however, they collected the samples for estradiol estimation on 7th day of menstrual cycle in premenopausal women unlike the present study, in which samples were collected irrespective of the day of menstrual cycle.[11]

According to Ettinger *et al*., serum estradiol levels vary with age with levels decreasing as age progresses and as the serum levels fall into the postmenopausal range (30 pg/mL), accelerated bone loss ensues. Women with



Graph 1: Correlation of mean serum estradiol (pg/ml) with mean cortical width (mandibular index) (mm) in Group C



Graph 2: Correlation of mean serum estradiol (pg/ml) with mean antegonion index (mm) in Group C

undetectable estradiol levels (5 pg/mL) were about 2.5 times more likely to suffer hip or vertebral fracture than women with detectable levels (5–25 pg/mL).[12]

There are many studies directly or indirectly correlating the markers of estradiol with bone mineral density in postmenopausal women.[9-11,13]

None of the radiographic parameters evaluated in the present study correlated with serum estradiol except the cortical width and AGI with which it showed positive correlation in Group C, i.e., postmenopausal women with periodontitis. This difference can be attributed to the possibility that estradiol is a marker for other confounding factors that we did not measure in the present study. We did not adjusted our measurements for the estradiol binding protein and sex hormone binding globulin in present study.

The reason for nonsignificant statistical difference in mean serum calcium and estradiol levels and various morphometric indices in this study in patients with Group "B" in spite of Group B included, postmenopausal women could be the effects of periodontitis and local osteolytic factors present in the Group C patients affecting the results. This needs further research while considering local effects of all the osteolytic enzymes.

The results of the present study serve once more to show the evidence of the decrease in cortical width, superior and inferior panoramic mandibular indices, and GI along with estradiol levels in postmenopausal women and thus can act as an adjunctive tool in deciding whether to refer such patients for further evaluation through bone density measurements through DXA scan.

Conclusion

Thus, it can be concluded from the present study that radiomorphometric indices cannot be used for diagnosing the patients with osteoporosis but can be used as a supplement to refer women with pronounced thinning or resorption of the inferior mandibular cortices for further investigation of osteoporosis. There is a little evidence of correlation of these indices with serum estradiol and calcium levels and therefore detailed further study and research about this correlation; and to use them for osteoporosis risk assessment, may help in creating an economic alternative of BMD measurements.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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