



Relation between Osteocalcin serum level and panoramic indices in osteoporotic patients



Eman Showky, Una El-Shinnawi, Galal El-Hawary, Tamer EL-Said,

Abstract:

This paper presents a correlation between the panoramic indices measured on the mandible and osteocalcin serum level. A **forty-five** female patients were involved in the study. **Group 1 (case group):** 15 female postmenopausal osteoporotic patients. **Group 2 (control group):** 30 female patients who were never known to be osteoporotic and was sub-grouped into **Subgroup 2A:** 15 female patients who were in premenopausal stage and **Subgroup 2B:** 15 female patients who were in the postmenopausal stage. **DEXA** scan was done for all patients to assess bone density. **Panoramic** views were made for all patients for different dental treatment aims. Informed consent was taken from all patients. A blood sample was collected from each patient after instructing them to fast for 12 hours prior to admission to our dental clinic at faculty of dentistry as outpatients. Osteocalcin levels were measured by liquid chromatography– tandem mass spectrometry ⁽¹⁾The correlation between panoramic indices and osteocalcin serum level was determined. The results shows a significant positive correlation between the gonial index (GI) on the left side of the mandible and serum osteocalcin level in the study group ($p=0.04$). There was a significant positive correlation between Antegonial index (AGI) on the left side of the mandible and serum Osteocalcin level in control 2A group ($p=0.09$). There was no significant correlation between any of the panoramic mandibular measurements and serum Osteocalcin level in control 2B group.

Introduction

Bone Densitometry (DEXA), considered the gold standard in both the diagnosis and monitoring of osteoporotic patients, but this diagnostic method is not often available in basic health services ⁽²⁾. The latest data from the literature have been suggesting an alternative to the use of DEXA in the clinical monitoring of OP patients: biomarkers of bone resorption and formation. Bone turnover can be effectively estimated, regularly with self analyzers, utilizing an assortment of biochemical markers in serum or urine. Biochemical markers of bone turnover are widely separated into two divisions: markers of bone resorption, which represent osteoclast action and are for the most portion debasement items of the sort I collagen and markers of bone-building that indicate osteoblast action and are byproducts of collagen formation, framework proteins or osteoblastic proteins. Bone resorption and bone synthesis are coupled forms, and subsequently, in most circumstances, any of these markers will indicate alter in bone turnover ⁽²⁾.

Panoramic radiography, Most of the post-menopausal ladies have more chances to visit a dental clinic for the curing of dental caries and periodontal infection than to visit therapeutic office for diagnosis of osteoporosis before fracture occurs ⁽¹³⁾. Therefore, panoramic radiograph plays a crucial importance in recognizing post-menopausal women with undiscovered osteoporosis. In this manner, early prediction by dentists would allow the essential preventive treatment to be initiated ⁽¹⁴⁾. The inferior mandibular cortical width was examined utilizing four additives (quantitative) parameters, named as **Mental index (MI), Mandibular Panoramic Index (MPI), Antegonial index (AI) and Gonial index (GI)** ⁽¹⁴⁾

Patients and Methods

Total of 45 female patients were given informed consent grouped as follow: **Group 1 (study group):** 15 female

osteoporotic postmenopausal patients. **Group 2 (control group):** 30 female patients who were never diagnosed as osteoporotic patients who seeking various dental treatments that needed panoramic and cone-beam CT radio graphical examination. They were sub grouped as follow: **Subgroup 2A:** 15 female patients who were in the premenopausal stage. **Subgroup 2B:** 15 female patients who were in the postmenopausal stage. Exclusion criteria were metabolic bone disorders as osteomalacia, diabetes, hyperparathyroidism. Drugs that affect bone turnover as steroids and anti-convulsions.

Panoramic Radiography:

Panoramic Digital x-rays were captured by a calibrated single technician. It was done by utilizing an Orthopantomograph 200 D (Instrumentarium Dental, Inc, Milwaukee, WI). Kilovoltage of 57 to 85 peak and a tube current of 12 to 16 mA was set. Patient's head alignment will be adjusted according to instructions of the manufacturing. All images were evaluated so that involving only the x-rays of perfect resolution and correctly positioned radiographs. Panoramic linear measurements were made by analytical software. The radiographs were assessed by two blinded radiologists. ⁽¹⁵⁾.

Qualitative mandibular index:

This index indicates the morphology of mandibular cortex and the degree of its porosity. This index has three types, referring to basic definitions described by **Klemetti et al.**, ⁽¹⁵⁾ as appears in figure 1:

- **MCI1:** It is a regular cortex and has sharp, even cortical margin is even, sharp on the right and left sides.
- **MCI2:** It is mild resorbed and moderately porous cortex. It occurs if there are semilunar defects on the cortical edge on either or both sides.

- **MCI 3:** It shows a weekend cortex, where the cortical layer has massive cortical cracklings and is so permeable.

Panoramic Quantitative Indices

Mandibular Inferior cortical width was evaluated using four additional (quantitative) values including

- **Mental index (MI).** Cortical width measure within the area of mental foramen and was evaluated referring to **Ledgerton et al.** principal ⁽¹⁶⁾. Values were gained through drawing a line on a right angle to mandibular lower border, crossing 1 cm behind MI (PMI1), 2 cm back to MI (MPI2) and 3 cm behind MI (PMI3).

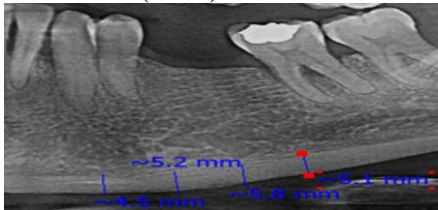


Figure (1) showing MI 1,2 and 3

- **Mandibular Panoramic Index (MPI) :**

It is the proportion of mandibular cortical width estimated on a line orthogonal on the mandibular bottom at the mental foramen centre to the linear measurement in-between the upper border of the mandibular cortex and bottom of the mandibular body. Its normal measure is above 0.3mm⁽¹⁷⁾

- **Antegonial index (AI):**

It is the estimation of the width of mandibular cortex estimated on a line perpendicular on the mandibular bottom at a crossing point with a tangent line to the anterior ramus border. Its usual measure is more than 3.2mm⁽¹⁸⁾.

- **Gonial index(GI):**

It is the width of mandibular cortex estimated on a bisector of that angle formed by the tangent line to the posterior ramus margin and mandibular inferior cortex. Its measure is more than 1.2mm normally⁽¹⁹⁾.

Osteocalcin serum level assessment

A blood sample was collected from each patient after instructing them to fast for 12 hours prior to admission to our dental clinic at faculty of dentistry as outpatients. Baseline blood samples will be frozen at -80 C and stored for osteocalcin levels were measured by liquid chromatography– tandem mass spectrometry ⁽¹⁾.

Serum sample preparation

After collection of the whole blood, it was allowed to clot by leaving it undisturbed at room temperature. This usually took 10-20 minutes. The clot was removed by centrifuging at 2,000-3,000 rpm for 20 minutes.

Statistical Analysis: The relationships between panoramic qualitative measurements, CBCT linear measurements and BMD measured by DEXA scan were determined by linear regression analysis, and the intraobserver agreement was examined using the Pearson correlation coefficient and Spearman's rho on SPSS 16.0 (SPSS Inc, Chicago, IL, USA) for Window.

Results

	Among cases	Mean \pm SD	Agreement
Study Group Osteocalcin level (24.2 \pm 5.86)	Qualitative mental index (right side) C1 C2 C3	Number 1 2 12	r=-0.17, P=0.54
	P value	0.39	
	Qualitative mental index (left side) C1 C2 C3	0 5 10	r=-0.22, P=0.43
	P value	0.43	
	MI I right	11.52\pm0.83	r=-0.045, P=0.87
	MI I left	11.32\pm0.79	r=-0.21, P=0.44
	MI II right	10.07\pm0.78	r=-0.19, P=0.48
	MI II left	9.66\pm0.88	r=-0.28, P=0.30
	MI III right	9.07\pm0.56	r=-0.08, P=0.76
	MI III left	8.56\pm0.62	r=-0.304, P=0.27
	PMI right	2.80\pm0.26	r=-0.06, P=0.83
	PMI left	2.79\pm0.38	r=-0.09, P=0.74
	AGI right	4.71\pm0.65	r=-0.17, P=0.54
	AGI left	4.61\pm0.79	r=-0.17, P=0.54
	GI right	0.84\pm0.14	r=-0.16, P=0.57
	GI left	0.939\pm0.17	r=0.52, P=0.04*
	Control Group (2A) Osteocalcin level (4.11 \pm 2.68)	Qualitative mental index (right side) C1 C2 C3	3 7 5
P value		0.22	
Qualitative mental index (left side) C1 C2 C3		Number 4 6 5	r=-0.16, P=0.58
P value		0.63	
MI I right		12.41\pm1.57	r=0.35, P=0.21
MI I left		12.64\pm1.31	r=0.29, P=0.28
MI II right		10.6\pm1.92	r=0.440, P=0.14
MI II left		11.43\pm1.76	r=-0.028, P=0.92
MI III right		9.21\pm1.9	r=0.27, P=0.33
MI III left		9.53\pm1.86	r=-0.01, P=0.9
PMI right		2.85\pm0.74	r=0.28, P=0.31
PMI left		2.96 \pm 0.63	r=0.33, P=0.23

	AGI right	4.56±1.21	r=-0.45, P=0.09
	AGI left	4.54±1.33	r=-0.45, P=0.09
	GI right	1.46±0.47	r=-0.32, P=0.25
	GI left	1.32±0.34	r=-0.26, P=0.34
Control Group (2B) Osteocalcin level (11.73 ± 5.11)	Qualitative mental index C1 C2 C3	1 12 2	r=-0.02, P=0.96
	P value	0.57	
	Quantative index C1 C2 C3	Number 2 7 6	r=0.17, P=0.54
	P value	0.24	
	MI I right	13.1±1.4	r=0.17, P=0.54
	MI I left	13.07±1.33	r=0.04, P=0.89
	MI II right	11.62±1.63	r=0.38, P=0.17
	MI II left	11.28±1.58	r=-0.08, P=0.77
	MI III right	10.44±1.71	r=0.14, P=0.61
	MI III left	9.44±1.77	r=-0.079, P=0.78
	PMI right	3.10±0.56	r=-0.05, P=0.85
	PMI left	3.06±0.57	r=0.13, P=0.65
	AGI right	3.91±0.68	r=-0.11, P=0.71
	AGI left	3.99±0.96	r=-0.06, P=0.83
	GI right	1.13±0.36	r=-0.09, P=0.75
	GI left	1.09±0.43	r=-0.01, P=0.98

[The relation between Osteocalcin serum level and panoramic mandibular measurements in the study group.](#)

Table (1) showing the mean and SD OF serum Osteocalcin level in the study group was **(24.26±5.86)**. There was no significant correlation between any of the panoramic mandibular measurements and serum Osteocalcin level except with the gonial index on the left side of the mandible where there was a positive correlation with Osteocalcin level (**p=0.04**).

[The relation between Osteocalcin serum level and panoramic mandibular measurements in control 2A group.](#)

the mean and SD of Osteocalcin serum level in control 2A group was **(4.11±2.68)**. There was no significant correlation between any of the panoramic mandibular measurements and serum Osteocalcin level except with the Antegonial index (AGI) on the left side of the mandible where there was a positive correlation with Osteocalcin level (**p=0.09**).

[The relation between Osteocalcin serum level and panoramic mandibular measurements in control 2B group.](#)

the mean and SD of Osteocalcin serum level in control 2B group was **(11.73±5.11)**. There was no significant correlation between any of the

panoramic mandibular measurements and serum Osteocalcin level.

Discussion: This study was made to discover any correlation between measures made on panoramic radiography and serum osteocalcin level. Thus, osteoporotic patients can be assessed by dental radiographs as a diagnostic aid. Bone biomarkers play an important role in understanding the pathogenesis of osteoporosis. Thus, those biomarkers were studied to evaluate their ability to predict osteoporosis. Osteocalcin is synthesized during bone formation secreted by osteoblasts^(20,21) and depending on calcium level. In osteoporosis, there is calcium deficiency and thus hydroxyapatite crystal formation is decreased, so the osteocalcin level is increased^(22,23)

In our study, we searched for a correlation between osteocalcin serum level with panoramic indices for osteoporosis. We found a significant correlation between serum osteocalcin level and gonial panoramic index on the left side of the mandible in the study group ($p=0.04$). There was a significant positive correlation between antegonial index on the left side of the mandible and serum osteocalcin level in control 2A group ($p=0.09$).

On the other hand, there was no significant correlation between osteocalcin level and Other panoramic indices. Those results come inconsistently with the study done by Kalaiselvi VS et al.⁽²⁴⁾ who found a negative correlation between osteocalcin level and BMD measurement of bone density. The osteoporotic case can be predicted by a combination of BMD measurement by DEXA and serum biomarker levels for confirming the diagnosis. Biomarker levels are used mainly for evaluation of treatment response and prognosis⁽²⁵⁾.

Conclusion

In this paper, panoramic indices showed a somewhat correlation with serum osteocalcin level and thus can be used to assess bone quality in postmenopausal females. Patients with lower panoramic indices should be referred to make DEXA measures for confirming osteoporotic status.

References

- 1- Dresner-Pollak R, Parker RA, Poku M, Thompson J, Seibel MJ & Greenspan SL (1996) Biochemical markers of bone turnover reflect femoral bone loss in elderly women. *Calcif Tissue Int* 59, 328–333
- 2- Grey A, Bolland M, Wong S, Horne A, Gamble G, Reid IR. Low-dose zoledronate in osteopenic postmenopausal women: a randomized controlled trial. *J Clin Endocrinol Metab*. 2012; 97(1)286-92.
- 3- Schneider DL & Barrett-Connor EL (1997) Urinary Ntelopeptide levels discriminate normal, osteopenic, and osteoporotic bone mineral density. *Arch Intern Med* 157, 1241–1245.
- 4- Hui SL, Slemenda CW & Johnston CC Jr (1990) The contribution of bone loss to postmenopausal osteoporosis. *Osteoporos Int* 1, 30–34
- 5- Dobnig H, Sipos A, Jiang Y, Fahrleitner-Pammer Ste-Marie LG, Gallagher JC, Pavo I, Wang J & Eriksen EF (2005) Early changes in biochemical markers of bone formation correlate with improvements in bone structure during teriparatide therapy. *J Clin Endocrinol Metab* 90, 3970–3977.
- 6- Rogers A, Hannon RA & Eastell R (2000) Biochemical markers as predictors of rates of bone loss after menopause. *J Bone Miner Res* 15, 1398–1404.
- 7- Uebelhart D, Schlemmer A, Johansen JS, Gineyts E, Christiansen C & Delmas PD (1991) Effect of menopause and hormone replacement therapy on the urinary excretion of pyridinium cross-links. *J Clin Endocrinol Metab* 72, 367–373.
- 8- Bauer DC, Sklarin PM, Stone KL et al. (1999) Biochemical markers of bone turnover and prediction of hip bone loss in older women: the study of osteoporotic fractures. *J Bone Miner Res* 14, 1404–1410.
- 9- Garnero P, Sornay-Rendu E, Duboeuf F & Delmas PD (1999) Markers of bone turnover predict postmenopausal forearm bone loss over 4 years: the OFELY study. *J Bone Miner Res* 14, 1614–1621.
- 10- Delmas PD, Christiansen C, Mann KG, Price PA. 1990. Bone Gla protein (osteocalcin) assay standardization report. *J Bone Miner Res* 5:5–11
- 11- Cantatore FP, Corrado A, Grano M, Quarta L, Colucci S, Melillo N. 2004. Osteocalcin synthesis by human osteoblasts from normal and osteoarthritic bone after vitamin D3 stimulation. *Clin Rheumatol* 23:490–495
- 12- Hauschka PV, Lian JB, Cole DE, Gundberg CM. 1989. Osteocalcin and matrix Gla protein: Vitamin K-dependent proteins in bone. *Physiol Rev* 69:990–1047.

- 13- Roberts M., Yuan J., Graham J., Jacobs R., Devlin H. (2011) Changes in mandibular cortical width measurements with age in men and women. *Osteoporos Int*; 22:1915–1925.
- 14- Otagoto, J. & Ota, N. Correlation between periodontal disease and osteoporosis using panoramic radiographic parameters for diagnosed osteoporosis in dental clinic. *Clin. Calcium.*, 13(5):582-6, 2003.
- 15- Klemetti E, Kolmakov S, Kröger H. Pantomography in assessment of the osteoporosis risk group. *Scand J Dent Res* 1994; 102: 68–72.
- 16- Ledgerton D, Horner K, Devlin H, Worthington H. Panoramic mandibular index as a radiomorphometric tool: an assessment of precision. *Dentomaxillofac Radiol* 1997; 26: 95–100. doi: 10.1038/sj.dmfr.4600215
- 17- Mohammad, A. R.; Alder, M. & McNally, M. A. A pilot study of panoramic film density at selected sites in the mandible to predict osteoporosis. *Int. J. Prosthodont*, 9:290-4, 1996.
- 18- Mohajery, M. & Brooks, S. L. Oral radiographs in the detection of early signs of osteoporosis. *Oral. Surg. Oral. Med. Oral. Pathol.*, 73:112-7, 1992
- 19- Halling A, Persson GR, Berglund J, Johansson O, Renvert S. Comparison between the Klemetti index and heel DXA BMD measurements in the diagnosis of reduced skeletal bone mineral density in the elderly. *Osteoporos Int* 2005; 16: 999–1003. doi: 10.1007/s00198-004-1796-x
- 20- Hamdi RA. Evaluation of Serum Osteocalcin level in Iraqi Postmenopausal women with primary osteoporosis. *J Fac Med Baghdad*. 2013;55(2):166-69.
- 21- Civitelli R, Armamento- Villareal R, Napoli N. Bone turnover markers: understanding their value in clinical trials and clinical practice. *Osteoporosis Int*. 2009;(20):853-51.
- 22- Jagtap VR, Ganu JV, Nagane NS. BMD and serum intact osteocalcin in postmenopausal osteoporosis women. *Ind J Clin Biochem*. 2013;26(1):70-73
- 23- Filip RS, Zagorski. Age and BMD related differences in biochemical markers of bone metabolism in rural and urban women from Lublin region, Poland. *Ann Agric Environ Med*. 2004;11:255-59.
- 24- Kalaiselvi VS, Prabhu K, Ramesh M, Venkatesan V. The Association of Serum Osteocalcin with the Bone Mineral Density in Post Menopausal Women. *Journal of Clinical and Diagnostic Research*. 2013;7(5):814-16
- 25- Bhattarai T, Bhattacharya K, Chaudhuri P, Sengupta P. Correlation of common biochemical markers for bone turnover, serum calcium, and alkaline phosphatase in post-menopausal women. *Malays J Med Sci*. 2014;21(1):58-61.