Print ISSN: 2321-6379
Online ISSN: 2321-595X
DOI: 10.17354/ijss/2016/626

Original Article

Comparison of Bone Biomarkers in Postmenopausal Women

Sunithapriya[1], Thirumalaipandiyan[2], Sasivathanam[3]

[1]Assistant Professor, Department of Biochemistry, Thanjavur Medical College, Thanjavur, Tamil Nadu, India, [2]Assistant Professor, Department of Orthopaedics, Thanjavur Medical College, Thanjavur, Tamil Nadu, India, [3]Professor, Department of Biochemistry, Thanjavur Medical College, Thanjavur, Tamil Nadu, India

Abstract

Introduction: Osteoporosis is a skeletal disorder characterized by reduced bone strength and increased susceptibility to fractures secondary to minor trauma. Major sequelae include fragility of bone and increased predisposition to fractures such as vertebral crush fracture, femoral neck fracture, and colles' fracture.

Aims and Objectives: The present study aims to understand the bone markers in postmenopausal women. In this study, we measured N-telopeptide, calcium, phosphorus, and alkaline phosphatase (ALP) levels in postmenopausal women and compared it with premenopausal women.

Materials and Methods: Study group included postmenopausal women aged 50-70 years who had bone mineral density (BMD) T-score ≥ - 2.5 and T-score between −1.0 and −2.5 and they were recruited from orthopedics outpatient department. Control group includes premenopausal women aged 25-35 years without any specific illness. Serum N-telopeptide was measured by ELISA method. Calcium, phosphorus and total ALP were measured in fully automated analyzer by chemical methods. BMD was assessed by ultrasonography taken in heel and the T-scores were recorded.

Statistical Analysis: Results were expressed as mean±standard deviation and were statistically analyzed using SPSS software version 16 and MS Excel. Student's *t*-test was used to analyze the difference between the two groups. The relationship between the variables was evaluated using Pearson's correlation coefficient. A $P < 0.05$ was considered to be statistically significant. The mean range of serum N-telopeptide in the study group (101.47 nmol BCE/L) is significantly higher than the control group mean (17.35 nmol BCE/L), and the *P* value is statistically significant. Pearson's correlation studies showed a positive correlation between N-telopeptide and total alkaline phosphatase, which is statistically significant.

Conclusion: Our findings show that there is a significant increase in serum N-telopeptide level in postmenopausal women when compared to other bone biomarkers and it correlates well with the degree of osteoporosis.

Key words: Bone mineral density, Calcium, N-telopeptide, Phosphorus, Postmenopausal osteoporosis, Total alkaline phosphatase

INTRODUCTION

Osteoporosis is a metabolic disorder characterized by decreased bone mass and increased susceptibility to fractures secondary to trivial trauma.[1] In osteoporosis, there is a disturbed balance between bone resorption and bone formation with a decrease in the amount of normal mineralized bone. The World Health Organization (WHO) operationally defines osteoporosis as a bone density that falls 2.5 standard deviations (SDs) below the mean for young healthy adults of the same gender - also referred to as a T-score of −2.5.[2]

Access this article online

www.ijss-sn.com

Month of Submission : 10-2016
Month of Peer Review : 11-2016
Month of Acceptance : 11-2016
Month of Publishing : 12-2016

As our society is "aging" there is a considerable shift in the epidemiology of osteoporosis. WHO Technical Report Series-843-predicts a significant increase in fracture neck of femur among Asian population over a period. By 2050, osteoporosis will be a major demographic factor due to changes in lifestyle and the increase in survival rate of elderly. In most western countries, the peak incidence of

Corresponding Author: Dr. D. Thirumalaipandian, 121, Sundaram Nagar, 6th Street, Medical College Road, Thanjavur - 613 004, Tamil Nadu, India. Phone: +91-9442251286. E-mail: sunithapandiyan@gmail.com

osteoporosis occurs at about 70-80 years of age, whereas in India it may afflict those 10-20 years younger at the age of 50-60 years.

Why females are at risk of osteoporosis than male? The skeletal architecture in male has a different morphology than female that set them at lower risk for developing osteoporosis. The increased diameter of bone and greater muscle mass in men gives them more agility and padding in case of fall.[3]

In postmenopausal women, following ovarian failure, there is an absolute acceleration in the rate of bone resorption due to increased osteoclast recruitment leading to an exaggerated form of physiological bone depletion.[4,5] In women, the decrease in sex steroids at menopause accelerates the bone loss to about 2% per year for the first 5 years and then declines to 1% loss per year.[6,7] Although the principle cause of age-related osteoporosis is the continuing effects of estrogen deficiency; a further contribution is also provided by "calcium deficiency."[8,9]

The cause of calcium deficiency is complex and is related to age-related decrease in calcium absorption in the gut and also due to reduced effectiveness of vitamin D on stimulating calcium absorption in the intestine.[10] Further, menopause related acceleration in renal calcium excretion is also noted. This is due to decreased resorption of calcium in the distal convoluted tubule associated with the loss of estrogen stimulation of Ca^{++} ATPase.[11]

Most of the cases of osteoporosis are not diagnosed until a fracture occurs. A routine spinal radiograph in a symptomatic patient will not detect osteoporosis until 30% of bone is lost. Hence, a radiograph is not useful in the follow-up of progression of bone loss in osteoporotic patients.

National osteoporosis foundation recommends that the diagnosis of osteoporosis is to be made clinically by quantifying the bone mineral density (BMD).[12] Recently, new bone turnover markers have been used to get a better idea on bone microarchitecture.[13,14] One such bone resorption marker is N-telopeptide, a stable degradation end product from Type 1 collagen present in bone (Figure 1).[15]

In view of the above facts, the present study was done to understand the bone markers in postmenopausal women. In this study, we have investigated N-telopeptide, calcium, phosphorus, and alkaline phosphatase (ALP) levels in postmenopausal women and compared it with premenopausal women.

MATERIALS AND METHODS

The study was conducted at Thanjavur Medical College Hospital after getting approval from the Ethical Committee. Written informed consent was obtained from the participants before enrollment into the study.

The study group included postmenopausal women aged 50-70 years who had BMD T-score ≥ − 2.5 and T-score between −1.0 and −2.5 and they were recruited from orthopedics outpatient department. Control group includes premenopausal women aged 25-35 years without any specific illness.

Under aseptic conditions, 5 ml of venous blood was collected from each subject. The vacutainers containing the blood samples were kept at room temperature for 30 min and then centrifuged at 2000 g for 15 min for a clear separation of serum. The following parameters were estimated immediately after the serum was separated in fully automated analyzer.

1. Calcium
2. Phosphorus
3. Total alkaline phosphatase.

The remaining aliquot of serum was stored at −20°C in the deep freezer for estimation of serum N-telopeptide.

BMD was assessed by ultrasonography taken in heel and the T-scores were recorded.

Statistical Analysis

Results were expressed as mean±SD and were statistically analyzed using SPSS software version 16 and MS Excel. Student's *t*-test was used to analyze the difference between the two groups. Relationship between the variables was evaluated using Pearson's correlation coefficient. A $P < 0.05$ was considered to be statistically significant.

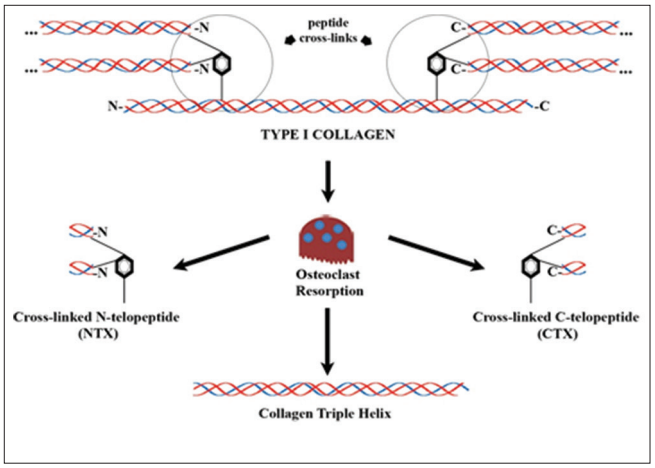

Figure 1: Formation of cross-linked N-telopeptide during osteoclast resorption

RESULTS

Table 1 and Figure 2 show mean N-telopeptide level between control and study group.

Mean serum N-telopeptide in the study group is 101.47 ± 18.39 nmol BCE/L which is higher than the control group mean 17.35 ± 3.2 nmol BCE/L which is statistically significant (*P* 0.0001 < 0.05).

Table 2 and Figure 3 show Student's *t*-test analysis of serum calcium, serum phosphorus, and the ionic product of calcium and phosphorus between control and study group.

In Table 2, there is a statistical decrease in mean serum calcium level in a study group of 9.30 ± 0.504 mg/dl when compared with mean serum calcium level in control group of 9.76 ± 0.529 mg/dl which is statistically significant.

Further, there is a statistical increase in mean serum phosphorus level in a study group of 3.976 ± 0.375 mg/dl when compared with mean serum phosphorus level in control group of 3.5728 ± 0.4855 mg/dl which is statistically significant.

Table 2 shows mean value of ionic product of calcium and phosphorus in the study group of 36.9 ± 3.27 which is higher when compared to study group of 34.72 ± 3.89 and it is statistically significant.

Table 3 and Figure 4 show a comparison of mean serum total ALP level between control and study group. Mean serum total ALP in study group is 105.62 ± 25.03 U/L which is higher than the control group mean serum total ALP 66.28 ± 12.02 U/L which is statistically significant.

Table 4 show Pearson's correlation between N-telopeptide and other study parameters.

Table 4 shows a positive correlation between N-telopeptide and total alkaline phosphatase, which is statistically significant.

DISCUSSION

Osteoporosis is a complex, multifactorial, polygenic disease in which genetic determinants are modulated by hormonal, nutritional, and environmental factors.

The present concept is that osteoporosis represents the continuum, in which multiple pathogenic mechanisms converge to cause loss of bone mass and microarchitectural deterioration of skeletal structure. These factors coupled

Table 1: Mean N-telopeptide level between control and study group

N-telopeptide	Mean±SD	Statistical inference
Control (*n*=50)	17.3504±3.23883	T=−31.840
Study (*n*=50)	101.4728±18.39896	0.0001<0.05
		Significant

SD: Standard deviation

Table 2: Student's *t*-test analysis of serum calcium, serum phosphorus and the ionic product of calcium and phosphorus between control and study group

Analyte	Mean±SD	Statistical significance
Calcium		T=4.451
Control (*n*=50)	9.7620±0.52911	0.0001>0.05
Study (*n*=50)	9.3020±0.50406	Significant
Phosphorus		T=−1.176
Control (*n*=50)	3.5728±0.48556	0.0001>0.05
Study (*n*=50)	3.9760±0.37502	Significant
Ca X P ratio		T=−3.040
Control (*n*=50)	34.72±3.893	0.03>0.05
Study (*n*=50)	36.90±3.279	Significant

SD: Standard deviation

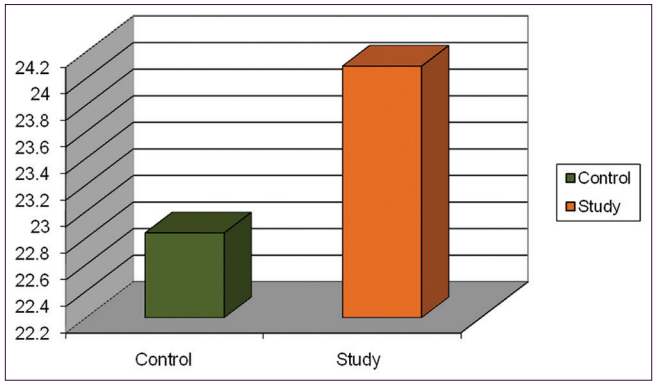

Figure 2: Mean N-telopeptide level between control and study group

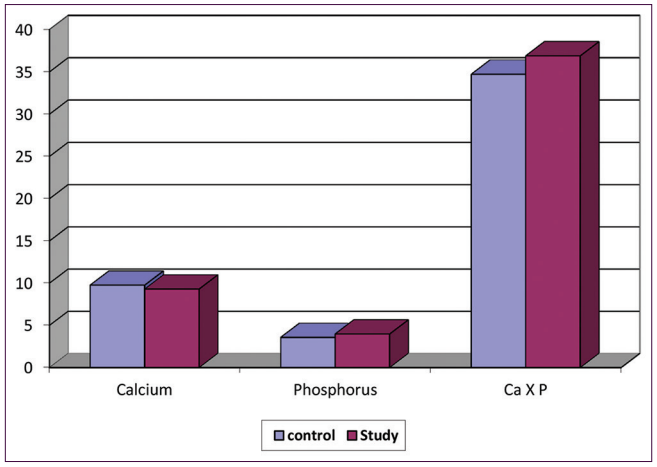

Figure 3: Student's *t*-test analysis of serum calcium, serum phosphorus, and the ionic product of calcium and phosphorus between control and study group

Table 3: Comparision of mean serum total ALP level between control and study group

ALP	Mean±SD	Statistical inference
Control (*n*=50)	66.28±12.026	T=−10.015
Study (*n*=50)	105.62±25.036	0.001<0.05
		Significant

ALP: Alkaline phosphatase, SD: Standard deviation

Table 4: Pearson's correlation between N-telopeptide and other study parameters

Study N-telopeptide	Correlation value	Statistical inference
BMD	−0.746 (**)	*P*<0.01 significant
Calcium	−0.238	*P*>0.05 not significant
Phosphorus	−0.015	*P*>0.05 not significant
Ca X P	−0.168	*P*>0.05 not significant
ALP	0.288 (*)	*P*<0.05 significant

**P*<0.05, ***P*<0.01. ALP: Alkaline phosphatase, BMD: Bone mineral density

with increased incidence of falls contribute to a high incidence of fragility fractures in osteoporotic patients.

Due to increased longevity of Indian population, now it is realized as in the west, the osteoporotic fractures are the major cause of morbidity and mortality in the elderly. The commonly used technique to diagnose osteoporosis and predict future fracture risk is an assessment of BMD by bone densitometry which is principally a measure of mineral content of bone. BMD measurements strongly correlate with load bearing capacity of hip and spine and also with the risk of fracture.[16]

However, the densitometric scan does not reflect the dynamic nature of bone tissue. In contrast, biochemical markers of bone turnover provide a better insight of bone growth, bone remodeling, and their measurement is useful in the assessment of metabolic bone diseases like osteoporosis and they provide an integrated evaluation of global disease activity rather than assessing a regional activity as with densitometric scan.[17,18]

In this present study, we have studied the bone resorption marker N-telopeptide along with other markers namely calcium, phosphorus, and total ALP in association with BMD in postmenopausal women and compared it with the premenopausal women.

Comparison of mean value of serum N-telopeptide of the study group (101.47 ± 18.39) with that of control group (17.35 ± 3.23) showed a significant rise in the study group. This shows that there is increased rate of bone resorption the following menopause. This study also correlates with the previous studies done by Jayaram *et al.*[19]

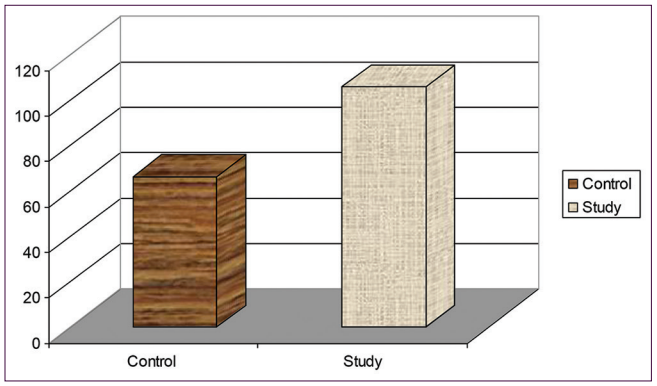

Figure 4: Comparision of mean serum total alkaline phosphatase level between control and study group

In this study, serum calcium, serum phosphorus, and serum total ALP shows no significant correlation with serum N-telopeptide, which in turn suggests that these parameters do not reflect the same aspects of bone metabolism as that of serum N-telopeptide.

With regard to serum calcium, the blood level is tightly regulated within normal limits by Parathyroid hormone otherwise, alterations in the homoeostasis of serum calcium may lead on to life-threatening complications.

Although there is a significant increase in the mean level of serum total ALP in the study group (105.62 ± 25.03) when compared to that of control group (66.28 ±12.02) it cannot be considered as a reliable marker for osteoporosis because it is not specific for bone. The blood level of serum total ALP is contributed by various tissues such as liver, placenta, intestine in addition to osteoblasts of bone.[20]

In the Pearson's correlation analysis, the serum N-telopeptide shows significant negative correlation with BMD and a positive correlation with serum total alkaline phosphatase.

These observations finally suggest that the level of serum N-telopeptide, the cross-linked collagen peptides increases with bone resorption and can be used as a reliable marker in primary postmenopausal osteoporosis. They appear as a promising tool for defining the skeletal status of postmenopausal women.

CONCLUSION

Our findings show that there is a significant increase in serum N-telopeptide level in postmenopausal women when compared to other bone biomarkers and it correlates well with the degree of osteoporosis. Further, measurement of serum N-telopeptide also helps to identify the high-risk individuals for fracture.

REFERENCES

1. Cosman F, Dempster D. Pathogenesis of osteoporosis. Metabolic bone diseases. In: Hochberg MC, Silman AJ, Smolen JS, Weinblatt ME, Weisman MH, editors. Rheumatology. 4th ed. Philadelphia, PA: Elsevier Publication; 2007. p. 193.
2. Chaudhary LJ, Kumar R. Osteoporosis: Investigations helping early diagnosis. Orthop Today 2010;12(1).
3. Dy CJ, Lamont LE, Ton QV, Lane JM. Sex and gender considerations in male patients with osteoporosis. Clin Orthop Relat Res 2011;469:1906-12.
4. Teitelbaum SL. Postmenopausal osteoporosis, T cells, and immune dysfunction. Proc Natl Acad Sci U S A 2004;101:16711-2.
5. Raisz LG. Pathogenesis of osteoporosis: Concepts, conflicts, and prospects. J Clin Invest 2005;115:3318-25.
6. Wali JP, Handa R, Aggarwal P. Osteoporosis. In: Sharma OP, editor. Geriatric Care in India. 3rd ed. New Delhi: Viva Books; 2008. p. 305-6.
7. Risteli J, Winter WE, Kleerakoper M, Risteli L. Bone and mineral metabolism. In: Burtis CA, Ashwood R, Burns E, editors. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 5th ed. Philadelphia, PA: WB Saunders; 2012. p. 1778-80.
8. Solmon L. Metabolic and endocrine disorders. Apley's System of Orthopaedics and Fracture. 9th ed. London: Arnold Publications; 2010. p. 132-3.
9. Athanasou NA. Pathological basis of orthopaedic and rheumatic disease. Osteoporosis. London: Arnold Publications; 2001. p. 139-40.
10. Prince RL. Bone diseases in the elderly. In: Wass JA, Shalet SM, editors. Oxford Textbook of Endocrinology and Diabetes. New York: Oxford University Press; 2002. p. 1424.
11. Bukata SV, Roiser RN. Metabolic bone diseases and osteonecrosis. In: Greene WB, editor. Netters Orthopaedics. 1st ed. Philadelphia, PA: WB Saunders; 2006. p. 33-4.
12. Guise T, Heras-Herzig A. Osteoporosis and osteopenia. In: Miller MD, Hart JA, MacKnight JM, editors. Essential Orthopaedics. Philadelphia, PA: Saunders/Elsevier, 2010. p. 102.
13. Delmas PD, Genant HK. Bone density and imaging of osteoporosis. In: Jameson JL, De Groot LJ, editors. Endocrinology Adult and Pediatric. 6th ed., Vol. I. Philadelphia, PA: Saunders Elsevier Publication; 2015. p. 1280-1.
14. Garnero P, Hausherr E, Chapuy MC, Marcelli C, Grandjean H, Muller C, *et al*. Markers of bone resorption predict hip fracture in elderly women: The EPIDOS Prospective Study. J Bone Miner Res 1996;11:1531-8.
15. Becker S. Surgical operations in orthopaedic spine. In: Sivananthan S, Sherry E, Miller WP, editors. Mercer's Textbook of Orthopaedics and Trauma. 10th ed. London: Hodder Arnold Publication; 2012. p. 1027.
16. Mukherjee S. Investigations and Diagnosis of Bone Disorders. In: Munjal YP, editor. API Textbook of Medicine. 9th ed., Vol. I. New Delhi: Jaypee Publications; 2012. p. 302.
17. Huang Y, Eapen E, Steele S, Grey V. Establishment of reference intervals for bone markers in children and adolescents. Clin Biochem 2011;44:771-8.
18. Delmas PD, Vrijens B, Eastell R, Roux C, Pols HA, Ringe JD, *et al*. Effect of monitoring bonernover markers on persistence with risedronate treatment of Postmenopausal osteoporosis. J Clin Endocrinol Metab 2007;92:1296-304.
19. Jayaram N, Bijoor AR, Rajagopalan N, Venkatesh T. The value of serum and urinary N-telopeptide in the diagnosis of osteoporosis. Indian J Orthop 2002;36:1-5.
20. McCormick RK. Osteoporosis: Integrating biomarkers and other diagnostic correlates into the management of bone fragility. Altern Med Rev 2007;12:113-45.

How to cite this article: Sunithapriya, Thirumalaipandiyan, Sasivathanam. Comparison of Bone Biomarkers in Postmenopausal Women. Int J Sci Stud 2016;4(9):112-116.

Source of Support: Nil, **Conflict of Interest:** None declared.