

Study to Compare Serum Beta Crosslaps Levels Between Premenopausal and Postmenopausal Women

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ABSTRACT

Introduction: Osteoporosis is a progressive systemic disease of the bone causing significant reduction in bone mineral density and microarchitecture of bone tissue. All women experience slow bone loss with age. In Pakistan accelerated bone loss at menopause in women is about 75.3% increasing upto 97% with age thus making osteoporosis a major health problem. At the time of menopause, serum automated β -Crosslaps increases by 86% a pattern consistent with accelerated bone loss within the first few years following menopause. We therefore hypothesized that estimation and comparison β -Crosslaps levels in Premenopausal and Postmenopausal women may be used as a diagnostic and screening marker for prevention of postmenopausal osteoporosis.

Study Design: A cross sectional comparative study.

Place and Duration of Study: This study was conducted in department of Physiology, BMSI in collaboration with Karachi gymkhana through a medical campaign in September 2011

Materials and Methods: A total of 94 subjects (premenopausal and postmenopausal) were included in this study that was performed in the urban area of Karachi city in 2011. Data was collected from all subjects through a questionnaire including questions regarding their age, menstrual history, menopausal and medical history. Blood samples from all these subjects were collected for the determination of bone turnover marker beta crosslaps. Bone mineral density (BMD) of the heel bone was done by single x-ray absorptiometry.

Results: The results of our study showed that the levels of serum β -Crosslaps in postmenopausal women were significantly higher as compared to premenopausal women $p < 0.01$. There was a significant rise in the β -Crosslaps levels with the increasing age among the postmenopausal women $p < 0.01$. BMD (bone mineral density) value have negative correlation the beta crosslaps levels $p < 0.01$ i.e with the increasing age there was decrease in BMD value and increase in β -crosslaps values.

Conclusion: Serum β -crosslaps levels in postmenopausal women can provide valuable information regarding the decreasing bone density and hence may be considered a cost effective diagnostic as well as screening marker for the prevention of postmenopausal osteoporosis.

Key Words: Crosslaps, Premenopausal, Postmenopausal

INTRODUCTION

Osteoporosis is a progressive systemic disease of the bone causing significant reduction in bone mineral density and micro architecture of bone tissue. All women experience slow bone loss with age. According to the study done by the National Osteoporosis Risk Assessment (NORA) on more than 200,000 healthy postmenopausal women revealed an unexpectedly high prevalence of osteopenia and osteoporosis, resulting in increased risk of fractures.¹

In Pakistan accelerated bone loss at menopause is about 75.3 increasing upto 97% with age thus making osteoporosis and related hip fractures a major health issue. Besides the diagnostic approaches i.e imaging techniques like DEXA, the risk of osteoporosis should be determined by a combination of measures that include BMD (bone mineral density) and level of bone

markers in early postmenopausal years in order to prevent osteoporosis. In elderly women, increased levels of biochemical markers of bone turnover, more specifically of bone resorption that have been associated with an increase risk of hip fracture independently of bone mineral density.² Presently the most authentic and widely used serum assay is the Elecsys β -crosslaps serum assay (Roche Diagnostics) which is a sandwich immunoassay with two monoclonal antibodies specific for Beta isomerized eight amino acid sequence i.e Glu-Lys-Ala-His- β -Asp-Gly-Gly-Arg linked by lysine residue, of the C-terminal telopeptide of type I collagen. This has proven to be a specific and sensitive marker of bone resorption in serum.³ It is a collagen decomposition product which is peptide in nature.⁴

At the time of menopause, serum automated β -Crosslaps (bone turnover marker) increases by 86% a

pattern consistent with accelerated bone loss within the first few years following menopause. The upper limit of the normal β -crosslaps value for healthy young women is 0.299 ng/ml and is 0.556 ng/ml in postmenopausal women.⁵. Hence estimation and comparison of β -Crosslaps levels in Premenopausal and Postmenopausal women may be used as diagnostic and screening marker for prevention of postmenopausal osteoporosis.

MATERIALS AND METHODS

A Cross sectional study recruiting a total of 94 women equally divided in two groups, Premenopausal women (age 30-47 years) and Postmenopausal women (age 48 years and above) from the local population in order to explore the role of serum β -Crosslaps in relation to bone health.

The study was planned in way that a campaign was organized for women above 30 years of age .Posters inviting participants were also put up in the health club Karachi gymkhana where this campaign was held on the 9th and 10th of September 2011. All participants were ensured of complete confidentiality and were informed about the dissemination of the research findings .Formal consent was obtained from women who agreed to participate in the study .More than 140 women participated in the campaign a whole research team was organized in groups to take the consent ,fill the questionnaire specially designed for the study , collection of blood sample and finally for quantitative ultrasonography in order to determine the bone mineral density . Participants were selected not only on the basis of age and menopausal status but also history of use of glucocorticoids, antiresorptive therapies, use of hormone replacement therapies, pregnancy, lactation, total hysterectomy and any other chronic illness. Out of all these participants 94 women were selected as they fulfilled all the criteria of the study.

Blood samples were obtained in 4-5 ml serum separator tube. The tubes were then centrifuged at 1500 g for 10 minutes; the serum was separated and immediately frozen and stored in aliquots at -70°C pending analysis. Serum β -Crosslaps levels was determined from these samples. Bone Mineral Density (BMD) of the heel bone calcaneus was done by ultrasound bone densitometer. (Osteosys Sonost 3000 Bone Densitometry)

RESULTS

Obtained data was recorded and statistically analyzed through statistical package for social sciences (SPSS version 11). Clinical characteristics were summarized in terms of frequencies and percentages for qualitative/categorical variable i.e. disease (osteopenia / osteoporosis) mean \pm S.D. for quantitative variables (BMD and β -Crosslaps). Student t-test/ANOVA was used for quantitative data. In all statistical analysis only p-value <0.05 are considered significant.

Table No.1: Comparison of beta crosslaps among both groups (pre and post menopausal women)

Variable	Group A Pre-menopausal (n=47)	Group B Post-menopausal (n=47)	P-value
	Mean \pm S.D	Mean \pm S.D	
β -CrossLaps (ng/mL)	0.23 \pm 0.13	0.54 \pm 0.15 *	0.001

* Statistically significant p<0.01

Table No.2: Comparison of radiological parameter among both groups (pre and post menopausal women)

Variables	Group A Pre-menopausal (n=47) Mean \pm S.D	Group B Post-menopausal (n=47) Mean \pm S.D	P-value
BMD - value	- 1.05 \pm 0.83	-1.60 \pm 0.75 *	0.001
BMD in %	80.6 \pm 15.37	72.0 \pm 14.11*	0.006

* Statistically significant p<0.01

Table No.3: Correlation (r) of beta crosslaps with radiological parameter

Parameters	Pre-menopausal women	Post-menopausal women
BMD - value	r = - 0.78 *	r = - 0.89 *
BMD in %	r = - 0.84 *	r = - 0.84 *

* Significantly negative correlation with Beta Crosslaps p<0.01

Table No.4: Correlation (r) of beta crosslaps with BMD in women

Beta crosslaps with abnormal BMD	r = - 0.61 *
Beta crosslaps with normal BMD	r = - 0.33

* Correlation is significant at the 0.01 level (2-tailed)

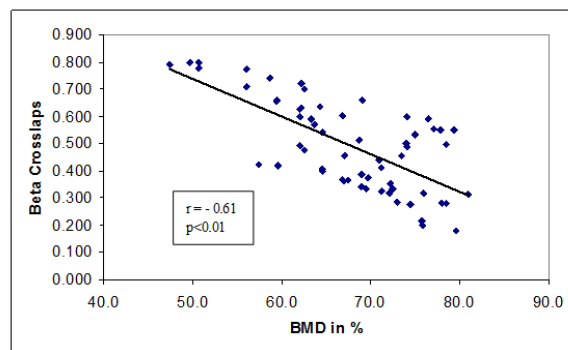


Figure No.1: Correlation (r) of beta Crosslaps with BMD

The results of our study showed that the levels of serum β -Crosslaps in postmenopausal women were significantly higher as compared to premenopausal

women $p < 0.01$. There was a significant rise in the β -Crosslaps levels with the increasing age among the postmenopausal women $p < 0.01$. BMD (bone mineral density) value have negative correlation with the β -Crosslaps levels i.e with the increasing age there was decrease in BMD value and increase in β -Crosslaps values.

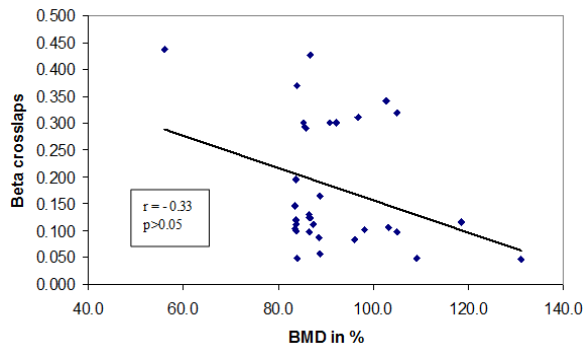


Figure No.2: Correlation (r) of beta cross laps with normal BMD in women

DISCUSSION

To proceed this study 94 women were selected from the local population of Karachi and were equally divided into two groups according to age and menopausal status, Group A comprised of Premenopausal women (ages 30-47 years) and Group B Postmenopausal women (ages 48 and above). Similar grouping can be seen in the study done by Jovcevska *et al.*⁵

In this study the quantitative ultrasound, Sonost 3000 bone densitometer was used for the determination of the bone mineral density of the heel bone (calcaneus) similarly Hans and Krieg⁶ have also supported the use of quantitative ultrasound for detection and management of osteoporosis and that the heel QUS appears to be most tested and most effective.

Fatima *et al.*⁷ suggested in their study the use of Calcaneal QUS for diagnosis of osteoporosis. This has been used by many other studies; it is considered to be a reliable assessment of bone density and has also been shown to predict fractures in elderly women. In a study conducted in Pakistan by Fahim⁸ by using the same device, 35.4% of the women were found to be osteopenic while 12.01% had osteoporosis.

Similarly, a preliminary survey done by Sharma *et al.*⁹ in India using calcaneal QUS showed the incidence of osteoporosis and osteopenia to be 20.3% and 36.8%, respectively, for women over the age of 45 years. After the age of 65 years, there was almost a 100% incidence in osteoporosis among women.

According to the World Health Organization criteria, individuals with a T-score of less than -2.5 are diagnosed as osteoporotic, those with a T-score of

between -2.5 and -1 as having a low bone density and at risk of osteoporosis (osteopenia) and a T-score of greater than -1.0 as normal.^{10,11}

In the conducted study it was observed that almost half of the women 51.1% in group A, premenopausal group (age 30-47 years) had T-scores between -2.5 to -1 and fall in the category of risk of osteoporosis (osteopenia) while the other half 48.9% had normal BMD with T-score greater than -1 and were taken as control. While among the healthy postmenopausal women in group B (age 48 years and above) 70.2% fall in the category of being at risk osteoporosis T-score between -2.5 and -1 , 21.3% had normal BMD (control) while only 8.5% had T-scores less than -2.5 (osteoporotic).

Likewise, Kim *et al.*¹² by using calcaneal QUS found that 34.2% of elderly Korean women had T-scores of between -1.0 and -2.5 , and 11.8% had T-scores of below -2.5 .

Siris¹³ reported that although osteopenic women, as individuals, have a more moderate risk than women with osteoporosis, there are far more people in this diagnostic category of osteopenia which is also apparent from the findings of our study more women in both groups fall in the category of osteopenia.

The levels of serum β -CrossLaps in our study were highly significant in group B postmenopausal women as compared to premenopausal women in group A. Similarly β -CrossLaps determined by the same method Elecsys in the study done by Garnero *et al.*¹⁴ was higher by 86% in postmenopausal women as compared to premenopausal women at the time of menopause a pattern steady with accelerated bone loss occurring within the first years following menopause Chailurkit *et al.*¹⁵, Jovcevska *et al.*⁵ and Okabe *et al.*³ also reported serum β -CrossLaps assay as a useful and non invasive method for determining bone remodeling in postmenopausal women and suggested that it cannot only be used to identify women at high risk for developing osteoporosis but can also be used to prevent it.

It was also shown from our study that increase of serum β -CrossLaps with age being highest in women age 65 years and above and is in the line with the findings supported by Jovcevska *et al.*⁵ study in which values of serum β -CrossLaps were highest in the older postmenopausal women.

A negative correlation of serum β -CrossLaps was seen with the bone mineral density values i.e. with the decreasing value of T-scores there was increase in serum β -CrossLaps values showing increase bone turnover thus predicting the future risk of developing osteoporosis and fractures related to it. This is in consonance with the study done by Ivaska *et al.*¹⁶ which showed the similar correlation of bone turnover markers with BMD and suggested serum β -CrossLaps

as the most consistent and significant bone resorption marker for identification of women with highest rate of bone loss and osteoporosis risk.

Comparable results with similar observation can be seen in Ofley study done by Sornay-Rendu *et al.*¹⁷ showing postmenopausal women with BMD values in the osteopenic range, a low BMD, an increased level of Bone turnover marker β -CrossLaps, predict the risk of vertebral and nonvertebral fractures up to 10 years later and also concluded that this may play an important role in identifying women at high risk of fracture who could not be adequately detected by BMD measurement alone While Garnero *et al.*¹⁸ in their study reported that bone resorption markers especially serum β -CrossLaps can predict osteoporotic fractures independently of BMD measured at several sites and concluded that combination of assessment of bone turnover marker and bone mineral density (BMD) can not only be helpful in identification of elderly women at high fracture risk but also young postmenopausal women.

CONCLUSION

Thus the findings of our present study suggest that Serum β -Crosslaps levels in postmenopausal women can provide valuable information regarding the decreasing bone density and hence may be considered as an adjunct in diagnosis of osteoporosis as well as cost effective screening marker for the prevention of postmenopausal osteoporosis. Further studies with large number of participants and more accurate assays should shed light to determine the usefulness of this bone resorptive marker in prevention of osteoporosis and its outcome.

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