Original Research Article

Serum Osteocalcin in Postmenopausal Women-A Pilot Study

ABSTRACT

Osteocalcin is a product of osteoblasts that is considerd a marker of bone formation. However osteocalcin is also released from bone matrix into blood during bone resorption, suggesting that osteocalcin is also a marker of bone turnover. Studies on this marker has shown both favouring and contradicting reports about different levels of steocalcin and ALP among postmenopausal women.

Aim and objective: To determine the diagnostic use of Osteocalcin and ALP in post menopausal women and to evaluate the association of osteocalcin in postmenopausal women.

Materials and methods: This was a cross sectional study with two groups of postmenopausal women. Group I of 20 subjects within first 5 yr after the onset of menopause and Group II of 20 subjects are of 5yr or more after the onset of menopause.serum uncarboxylated Osteocalcin, carboxylated Osteocalcin and ALP was estimated using ELISA technique.

Results: The serum ALP, carboxylated Osteocalcin(C-OC), uncarboxylated Osteocalcin (Uc-OC) values were higher in post-menopausal < 5years than those in > 5 years. ALP values correlated positively with C-OC but negatively with PM more >5 years(r=0.159: r= -0.369)

Conclusion: Bone turnover gets higher as the years progress among the post menopausal state which is reflected in ALP, Uc-OC and C-OC. More insight into this state is required to be studied with a larger sample size.

Keywords: [ALP, Bone Marker, Osteocalcin, Post menopause }

1. INTRODUCTION

Menopause is a phase frequently characterised by the skeletal mass diminution. The disproportionate change between bone formation and resorption is generally due to decreased utilisation/absorption of calcium and absence of ovarian function with lack of estrogen. Osteoporosis(OP), a major health problem in elderly population, especially in post-menopausal women, is diagnosed basically on clinical suspicion and bone mineral density measurement[1-3] Osteoporosis is a silent problem appearing as a part of ageing process observed in postmenopausal state,

Osteocalcin(OC) is a non-collagenous protein secreted from the bone[4] is synthesized in certain cells of the osteoblast lineage, mature osteoblasts and osteocytes[5,6]. Osteocalcin undergoes carboxylation reaction in presence of vitamin K to form carboxylatedosteocalcin (C-OC) and those which escape carboxylation are uncarboxylatedosteocalcin(Uc-OC). Apart from bone, it exists in blood circulation in small amounts hence may be considered a marker of bone turnover[7]. However, the role of OC in bone is not entirely understood. The marker is needed to detect the rapid loser of the bone tissue is osteocalcin. Bone loss is more rapid due to osteoporosis in postmenopausal women. During first 15-20 years after the onset of menopause nearly 30% of bone mass is lost due to osteoporotic changes [8-10]. The rate of bone loss is greater within first 5 years of the menopause as observed by Atalya et al in their study. It was also observed in their

study that total OC, Uc-OC, ratio of Uc-OC /OC and ALP levels in serum were significantly increased in osteoporotic women[11]
Similar observationswere also made in the previous studies in which total OC, Uc-OC levels in serum were significantly increased in post menopause phase than the premenopausal women[12,13]
Knapen et al showed that there was an inverse relation of serum Uc-OC/OC ratio and femoral neck BMD in first 10 yrs of postmenopause.[14]
Yasni et al in their study even though they formed that there were increased levels of serum. Uc-OC in perimenopausal women, but did not observe any association between L1-4 spine BMD and serum Uc-OC levels.[15]
Hence this study was undertaken to analyse serum levels of different forms of Osteocalcin in postmenopausal women.

2. MATERIAL AND METHODS

This study was carried out in the MRU-department in collaboration with Department of Biochemistry & Medicine. Post menopausal cases from out patients of medicine dept. were recruited for the study.These were divided into two groups group-I Post menopausal >5 years and group-II Post menopausal <5 years. Informed consent was obtained from all participants before initiating the study. Venous blood of 5 ml was drawn from patients. Carboxylated Osteocalcin(C-OC) and uncarboxylated Osteocalcin(Uc-OC) was analysed by kits obtained from DSS Takara Bio India Pvt. Ltd company and analysed by invitro-Enzyme Immunoassay using Biorad iMark Microplate reader. The Data was entered in Excel sheet. The statistical analysis was carried out with Statistical Package for Social Sciences for Windows ver. 11.0

Table 1: ALP, Uc-OC and C-OC levels >5 years &<5 years in Post Menopausal Women

		Median	p-value
More than 5 years	ALP(U/L)	38.00 (33-54)	0.088
Less than 5 years		87.00 (32-121)	
More than 5 years	C-OC (ng/mL)	4.799 (3.478-9.086)	0.562
Less than 5 years		5.65 (3.031-6.95)	
More than 5 years	Uc-OC (ng/mL)	1.38 (0.894-2.103)	0.606
Less than 5 years		1.869 (0.965-3.249)	

Values are expressed in Median (inter quartile range)

Table 2: Correlation between ALP, Uc-OC and C-OC between >5 years &<5 years

in Post Menopausal Women

		PM less than 5 years		PM More than 5 years	
		r-value	p-value	r-value	p-value
ALP	C-OC	0.609	0.047	0.159	0.640

ALP	Uc-OC	0.564	0.07	-0.369	0.264
C-OC	Uc-OC	0.400	0.223	0.018	0.958

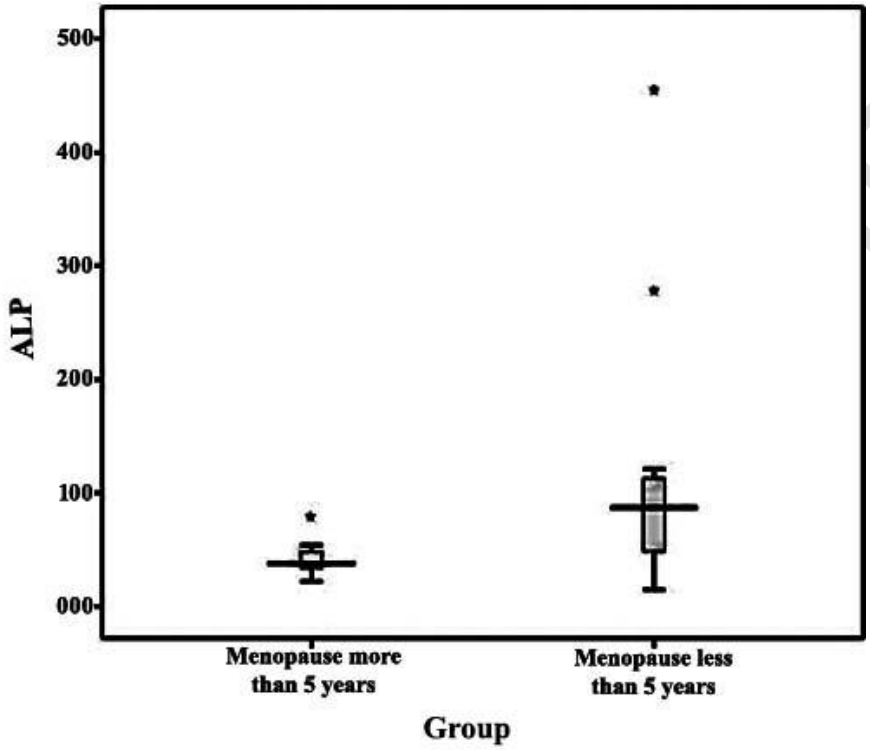

Fig 1: Box plot showing the distribution of ALP over PM>5 & PM<5 with outliers.

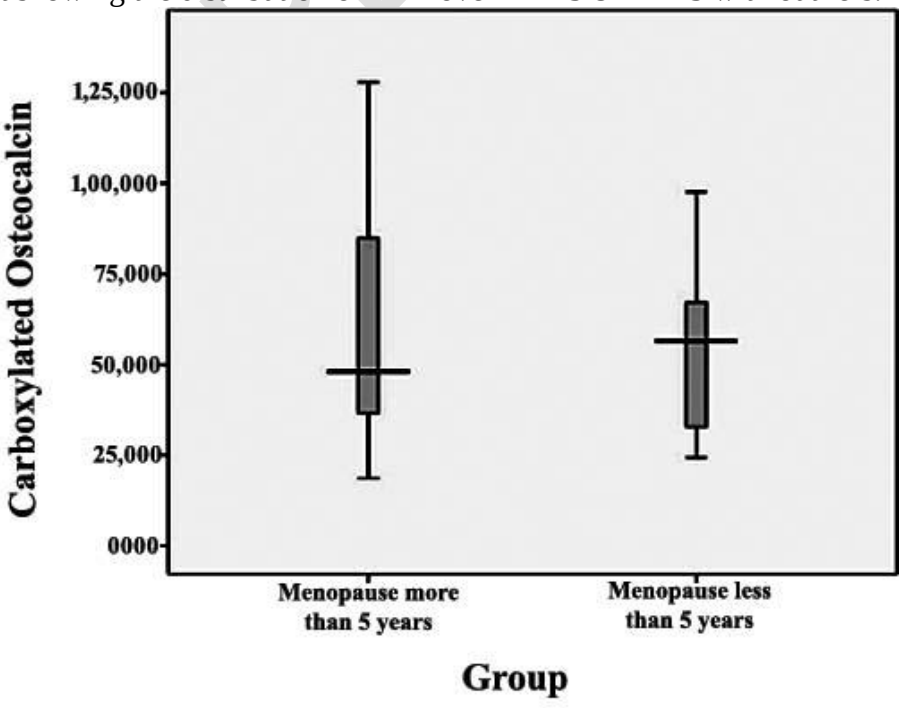

Fig 2: Box plot of ELISA results showing the distribution of C-OC over the PM>5 years & PM<5 years.

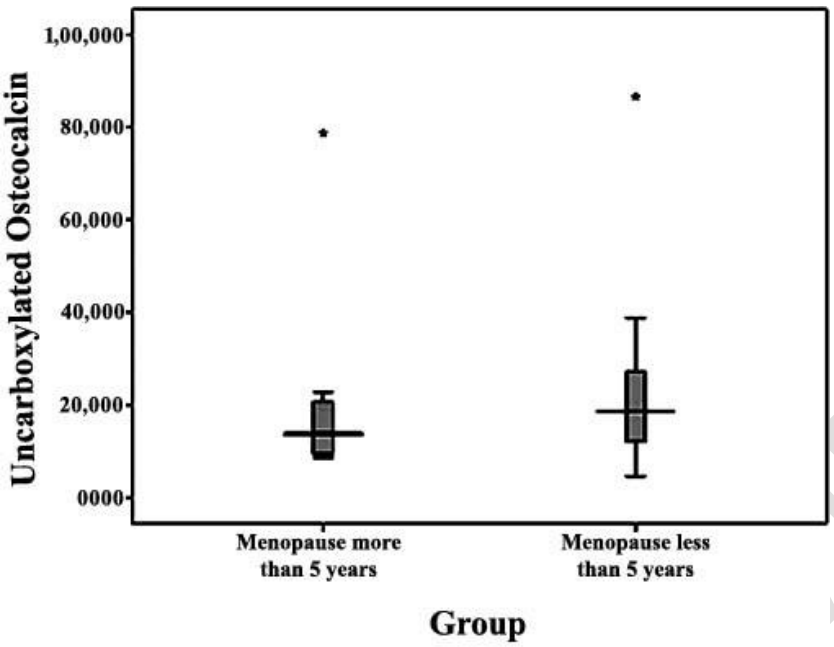

Fig 3: Box plot of ELISA results showing the distribution of uncarboxylated osteocalcin over the Post Menopause >5 years & <5 years.

3. RESULTS AND DISCUSSION

Osteocalcin is a product of osteoblasts that is considered a marker of bone formation [16].However, osteocalcin is also released from the bone matrix into blood during bone resorption, suggesting that osteocalcin is also a marker of bone turnover [17].Therefore, the higher serum osteocalcin levels and ALP observed in women within the first 5 yr after the onset of menopause may reflect an increased bone turnover rate rather than simply increased bone formation, and thus may be associated with an increased risk of bone fracture.

The current pilot study involved two groups; group-I Post-menopausal>5 years ([n=10) and group-II Post-menopausal<5 (n=8). As shown in Table no.1, the serum ALP values were higher in post-menopausal < 5years than those in > 5 years. Similarly both carboxylated osteocalcin (C-OC) and uncarboxylated Osteocalcin (Uc-OC) were higher in post-menopausal < 5years than those in post-menopausal > 5 years. The 'p' values of these were found satisfactory. As shown in Table no.2, Serum ALP correlated positively with carboxylatedosteocalcin and uncarboxylated osteocalcin with 'r' value of 0.609 and 0.564 respectively in Post-menopausal< 5 years group. Carboxylated osteocalcincorrelated positively with uncarboxylated osteocalcin with 'r' value of 0.400 in Post-menopausal< 5 years group.
Whereas in Post-menopausal>5 years group, Serum ALP correlated positively with carboxylatedosteocalcin and negatively with uncarboxylatedosteocalcin with 'r' value of 0.159 and -0.369 respectively and also carboxylatedosteocalcin showed positive correlation withuncarboxylatedosteocalcin with 'r' value of 0.018.
Plantalech et al. [12] reported that total OC and Uc-OC serum levels were significantly higher in postmenopausal women. As we observed in our study OC and Uc-OC levels were higher in post-menopausal < 5years than those in post-menopausal > 5 years including serum ALP levels.
A study by Szulc et al between post menopausal women and premenopausal control found that serum Uc-OC levels were elevated in 70-101 yrs old women and 23% had values higher than the premenopausal control group. [13]

4. CONCLUSION

In conclusion, our pilot study got a positive outcome which encourages and leads to proceed further for full-fledged study of osteocalcin in postmenopausal women.The bone turnover gets higher as the years progress among the post-menopausal state which is reflected in Uc-OC, C-OC and ALP.

The limitations of this study are, the number of the study population was low and the study did not measure other specific bone turnover markers that could support the importance of the first 5 yr after the onset of menopause for OP and OP therapy.

CONSENT (WHERE EVER APPLICABLE)

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for this study. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal.

ETHICAL APPROVAL (WHERE EVER APPLICABLE)

Ethical approval: Institutional Ethics Committee, Shimoga Institute of Medical Science, Shivamogga. Ref.No.:SIMS/IEC/369/2017-18

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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