

Original Research Article

A preliminary Study of Serum Osteocalcin in Postmenopausal Women

ABSTRACT

Osteocalcin is a product of osteoblasts that is considered a marker of bone formation. However, osteocalcin is also released from the bone matrix into the blood during bone resorption, suggesting that osteocalcin is also a marker of bone turnover. Studies on this marker have shown both favoring and contradicting reports about different levels of osteocalcin and **Alkaline Phosphate (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 10 subjects within first 5 yr after the onset of menopause and **Group II of 8 subjects following 5yr or more after** the onset of menopause. Serum uncarboxylated Osteocalcin, carboxylated Osteocalcin and ALP **were** estimated using the 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 larger sample size.

Keywords: (ALP, Bone Marker, Osteocalcin, Postmenopause)

1. INTRODUCTION

Menopause is a phase frequently characterized by skeletal mass diminution. The disproportionate change between bone formation and resorption is generally due to decreased utilization/absorption of calcium and the absence of ovarian function with a lack of estrogen. Osteoporosis(OP), a major health problem in an 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 the 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 carboxylated osteocalcin (C-OC) and those which escape carboxylation are uncarboxylated osteocalcin(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. **It may be needed to detect** the rapid loss of the bone tissue. Bone loss is **more rapid due to** osteoporosis in postmenopausal women. During the 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 the first 5 years of menopause as observed by Atalya et al in their study. It was also observed in their study that total OC, Uc-OC, a ratio of Uc-OC /OC and ALP levels in serum were significantly increased in osteoporotic women[11]

Similar observations were 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 the 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 analyze 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 the Department of Biochemistry & Medicine. Post menopausal cases from outpatients 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) were analyzed by kits obtained from DSS Takara Bio India Pvt. Ltd company and analyzed by invitro-Enzyme Immunoassay using Biorad iMark Microplate reader. The Data was entered into an 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 ^{NS}
Less than 5 years		87.00 (32-121)	
More than 5 years	C-OC (ng/mL)	4.799 (3.478-9.086)	0.562 ^{NS}
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 ^{NS}
Less than 5 years		1.869 (0.965-3.249)	

NS: Non-Significant

Values are expressed in median (interquartile range)

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

		<u>PM less than 5 years</u>		<u>PM More than 5 years</u>	
		r-value	p-value	r-value	p-value
ALP	C-OC	0.609	0.047	0.159	0.640 ^{NS}
ALP	Uc-OC	0.564	0.07 ^{NS}	-0.369	0.264 ^{NS}

C-OC	Uc-OC	0.400	0.223 ^{NS}	0.018	0.958 ^{NS}
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NS: Non-Significant

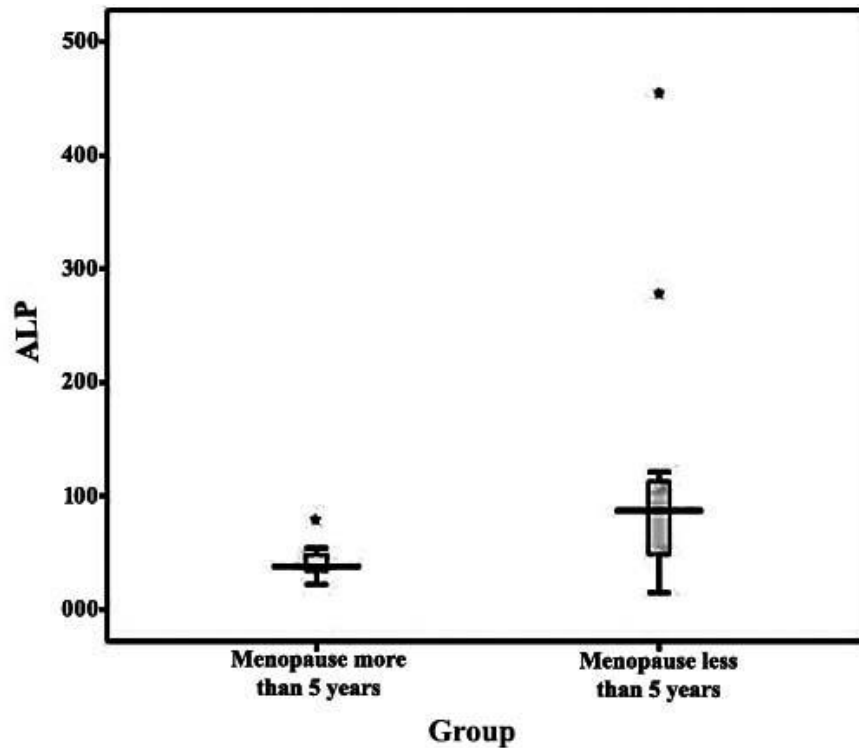


Fig 1: Box plot showing the distribution of ALP over PM>5 & PM<5 with outliers.

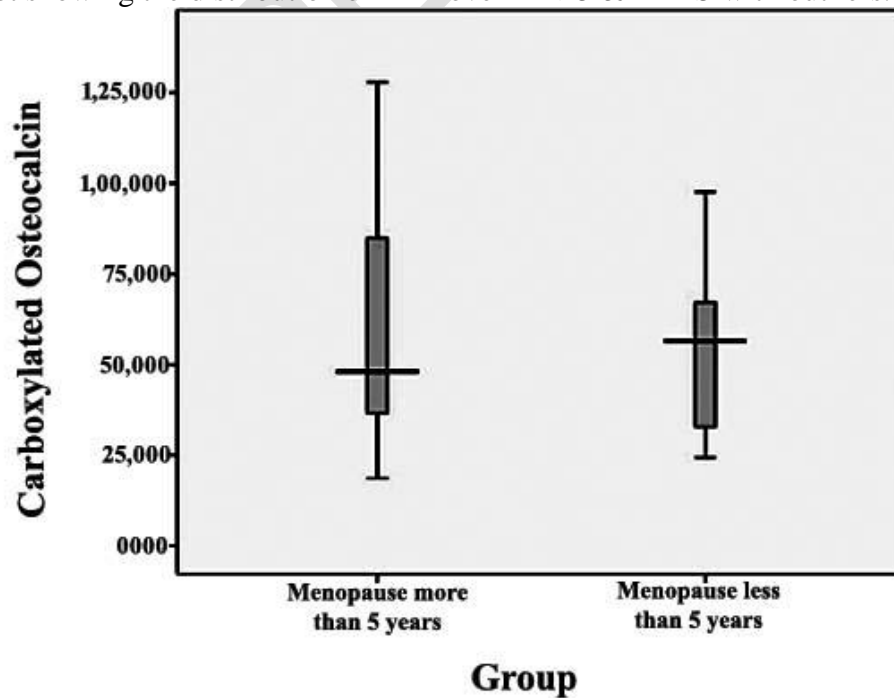


Fig 2: Box plot of ELISA results showing the distribution of C-OC over the PM>5 years & PM<5 years.

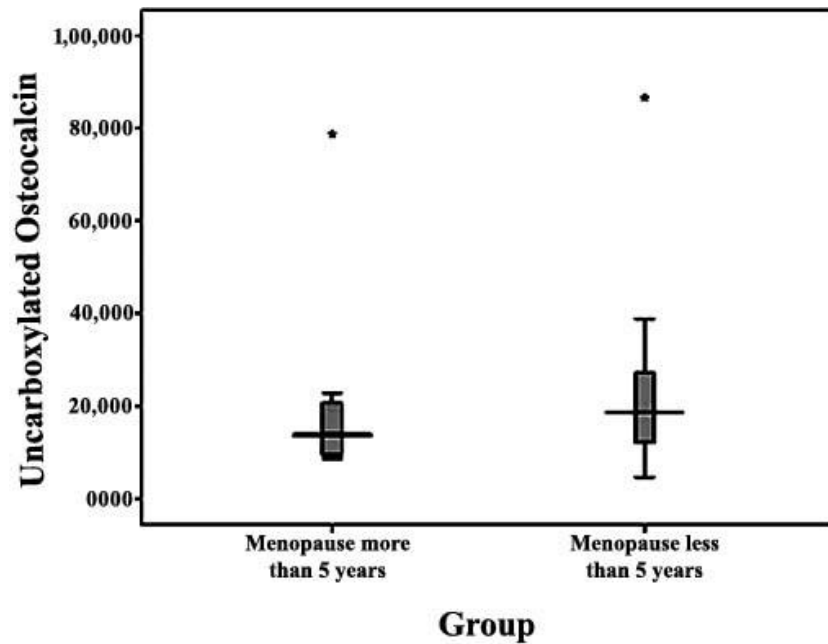


Fig 3: Box plot of ELISA results showing the distribution of uncarboxylated osteocalcin over the Post Menopause >5 years & <5 years.

3. RESULTS

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 not significant. As shown in Table no.2, Serum ALP correlated positively with carboxylated osteocalcin and uncarboxylated osteocalcin with 'r'-value of 0.609 and 0.564 respectively in Post-menopausal< 5 years group. Carboxylated osteocalcin correlated positively with uncarboxylated osteocalcin with 'r'-value of 0.400 in the Post-menopausal< 5 years group.

Whereas in the Post-menopausal>5 years group, Serum ALP correlated positively with carboxylated osteocalcin and negatively with uncarboxylated osteocalcin with 'r'-value of 0.159 and -0.369 respectively and also carboxylated osteocalcin showed a positive correlation with uncarboxylated osteocalcin with 'r'-value of 0.018.

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 the 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.

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 that encourages **and supports' proceeding to a fully-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.
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Conflict of Interest: Authors declare that there is no conflict of interest

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