Correlation Of Bone Turnover Markers With Age, BMI And Serum Oestradiol In Pre And Postmenopausal Urban Women

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Abstracts: Background: Rapid bone loss occurs in women after menopause due to hormonal factors that lead to an increased susceptibility to fractures. This study was done to find out the correlation of osteocalcin and telopeptide-C with age, body mass index (BMI) and oestradiol in premenopausal and postmenopausal women. Methodology**:** Study was conducted on 350 women aged 30–65 years who were classified into premenopausal and postmenopausal groups. Serum samples were analysed for oestradiol, osteocalcin and telopeptide-C. Pearsons correlation was used for statistical confirmations. Results: Osteocalcin was found to be correlated with age (r= +0.56, p<0.001), BMI (r= -0.39, p<0.001), oestradiol (r= -0.21, p<0.01) and telopeptide-C (r= +0.18, p<0.05) in postmenopausal women but no correlation was found in premenopausal women. Telopeptide-C was found to be correlated with age (r= +0.39,p<0.001), BMI (r= -0.29,p<0.001) and oestradiol (r= -0.48,p<0.001) in postmenopausal women; in premenopausal women it was found to be correlated with BMI (r= -0.30,p<0.001) and oestradiol (r= -0.29,p<0.001). Conclusion**:** Inverse correlation of Telopeptide-C with BMI and serum oestradiol in premenopausal and postmenopausal women suggests that their increased bone turnover was linked to low BMI and oestrogen deficiency.[Jain V NJIRM 2015; 6(2):66-69]

Key Words: Osteocalcin, Telopeptide-C, Postmenopausal women.

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Introduction: Osteoporosis is a systemic skeletal disease characterized by low bone mass and increased susceptibility to fractures. Osteoporotic fractures are a common cause of morbidity and mortality in adult Indian men and women.[1] Rapid bone loss is commonly seen in elderly individuals and tends to worsen with advancing age.[2] Bone mineral density (BMD) of women decreases with age, indicating bone loss with age and menopause.[3] In women rapid bone loss is seen after menopause and is found to be greatest in the early postmenopausal years.[4] Lack of estrogen accelerates this bone loss. [5]

Body weight has been found to be positively associated with BMD, from childhood through adulthood. This relationship is known to be stronger in older women.[6] Advancing age, menopause and low body mass index (BMI) being the primary risk factors of low BMD.[7] Low BMD is a significant risk factor for osteoporotic fractures later in life.[8] Early identification of women having low BMD is essential for giving them preventive treatment.[9]

BMD measures the rates of change in BMD at specific skeletal sites. Bone turnover markers (BTMs) reflect the whole body rates of bone resorption (resorption markers) and bone formation (formation markers). BTMs thus have an advantage over measuring BMD during early stages of bone loss as they provide a more representative index of the overall skeletal bone loss.[10] They provide valuable information for the diagnosis and monitoring of osteoporosis.[11] Early detection of future osteoporosis is important for its timely intervention. While BMD measurement has always been used for this purpose, additional measurement of BTMs has gained in importance for more effective monitoring.[12]

To date, there are very few Indian studies which indicate born turnover in our set up. Therefore this study was undertaken to find correlations of biochemical markers of bone turnover with age, BMI and serum oestradiol levels in premenopausal and postmenopausal women.

Material and Methods: This was a hospital based crossectional study conducted on 350 female subjects. The subjects were categorized into two groups; premenopausal and postmenopausal based on their menstrual history. The approvals of the Institutional Ethical Committee were obtained prior to conducting the research. Subjects were included in the study after obtaining their informed consent in local vernacular.

Questionnaires were filled in by the subjects. Their height, weight, calculated BMI, age at menarche, years since menopause in case of postmenopausal women, and history of disease were recorded. Women in pregnancy, lactating, or in postpartum period less than 12 months, carrying any disease or receiving treatment that could affect BMD; receiving/having received any treatment for osteoporosis; having a secondary cause for osteoporosis; suffering from chronic diseases affecting bone; undergoing current or had past treatment with drugs that could affect bone metabolism and those using oral contraceptive pills were excluded from the studies.

Five milliliters of blood was drawn from each subject. The serum was separated by centrifugation (3,000 rpm) within an hour of blood collection and was stored at −70°C for subsequent analyses. Before analyses, samples were allowed to attain the room temperature. The samples were analyzed for osteocalcin, telopeptide-C, and oestradiol by ELISA method.

The data obtained was analyzed using SPSS 16 software. The statistical test used was Pearsons correlation. The difference between the subjects was considered significant if the P value was less than 0.05.

Results: Osteocalcin was not found to be correlated with age, BMI and oestradiol in premenopausal women but in postmenopausal women it was found to be significantly correlated with age (+), BMI (-) and Oestradiol (-). **(Table - 1)**

Telopeptide-C was not found to be correlated with age in premenopausal women but it was found to be significantly correlated with BMI (-) and Oestradiol (-). In postmenopausal women Telopeptide-C was found to be significantly correlated with age (+), BMI (-) and Oestradiol (-). **(Table - 2)**

In premenopausal women Osteocalcin was not found to be correlated with Telopeptide-C (r= 0.009, P>0.05) but in postmenopausal women Osteocalcin was found to be positively correlated with Telopeptide-C (r= 0.181, P<0.05) (results not tabulated)

Table – 1: Correlation of osteocalcin with age, BMI and oestradiol .

Variables	Premenopausal		Postmenopausal	
	Correlation	P value	Correlation	P value
Age	0.160	NS	0.557	<.001
BMI	- 0.145	NS	- 0.396	<.001
Oestradiol	- 0.109	NS	- 0.208	<.01

Table – 2: Correlation of telopeptide-C with age, BMI and oestradiol.

Variables	Premenopausal		Postmenopausal	
	Correlation	P value	Correlation	P value
Age	0.036	NS	0.392	<.001
BMI	- 0.304	<.001	- 0.287	<.001
Oestradiol	- 0.296	<.001	- 0.478	<.001

Discussion: Present study could not find any significant correlation of age with serum concentrations of Osteocalcin and C-telopeptide in premenopausal women.[13,14,15] But in postmenopausal women, increase in Osteocalcin and Telopeptide-C in serum was found to be positively correlated with age, a pattern consistent with the accelerated bone loss occurring following menopause.[16, 17] Such a sustained bone turnover has been also found in other populations and with other bone formation and resorption markers.[18,12] Findings in present study indicate that bone resorption is increased in postmenopausal women when compared to premenopausal women. [14]

In the present study body weight or BMI is found to be inversely correlated with bone turnover markers i.e. women with a low body weight have high bone turnover, whereas overweight and obese women had low bone turnover and thus lower Serum Osteocalcin and Telopeptide as compared to those having normal weight.[19] High BMI has protective effect against bone loss.[20,21] The effect of obesity on fracture risk depends on its

definition. If defined on the basis of BMI, obesity may be protective against bone mineral loss or vertebral fracture. However, if obesity is based on the percentage of body fat, obesity may be a risk factor for osteoporosis.

In the present study in postmenopausal women Oestradiol was shown to be inversely correlated with bone turnover markers i.e. women with low oestrogen have high bone turnover. Decrease in oestradiol in postmenopausal women is because bone osteoblasts are more sensitive to age-related oestrogen loss than are the osteoclasts.[22] In premenopausal women Oestradiol was shown to be inversely correlated with bone resorption marker- Telopeptide-C. Oestrogen deficiency promotes bone loss at every age this is because it increases the life span of osteoclasts and decreases the life span of osteoblasts resulting in less bone formation.[23] These findings may be of relevance to the prophylactic treatment of low BMD with oestrogen replacement, since there is evidence to suggest that oestrogen can induce bone formation by increasing the production of osteoblasts.[24]
As reported in present study osteocalcin, marker of bone formation, and telopeptide-C, marker of bone resorption are positively correlated but actually both markers are expected to be negatively correlated.[14] Osteocalcin is released from bone-forming cells during bone formation and cleaved fragments are released from bone matrix during bone resorption. These cleaved fragments coexist in serum with intact peptide and may react with Osteocalcin antibodies in some assays. This heterogeneity limits its significance in clinical investigation of postmenopausal osteoporosis.[25] Methods which detect only intact osteocalcin and not the degraded fragments can explore the role of osteocalcin in diagnosis of postmenopausal osteoporosis.

Since in present study BTMs were measured irrespective of knowing the status of BMD, a follow up study can be conducted measuring both BMD and BTMs, to prove bone turnover markers as superior to measuring just BMD. Another limitation of the study was that it was hospital based study conducted on urban women and therefore results cannot be generalized to community and women living in rural areas. Further community based studies covering both rural and urban populations are suggested to overcome this limitation.

Conclusion: Inverse correlation of Telopeptide-C with BMI and serum oestradiol in premenopausal and postmenopausal women suggests that their increased bone turnover is linked to low BMI and oestrogen deficiency. Absence of significant correlation between bone formation marker with BMI and serum oestradiol in premenopausal women suggests that bone formation is influenced by either of these variables only when their values fall below a particular threshold value. Since high risk women have increased chance to develop osteoporosis, they should be identified at an early stage so that preventive measures can be taken and early interventions can be instituted if required. This will reduce morbidity and mortality associated with the disease.

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Conflict of interest: None
Funding: None
Cite this Article as: Dr Jain V, Dr Agrawal B, Dr Varshney A, Correlation Of Bone Turnover Markers With Age, BMI And Serum Oestradiol In Pre And Postmenopausal Urban Women. Natl J Integr Res Med 2015; 6 (2): 65- 68