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Research Article

Bone turnover markers in women can predict low bone mineral density

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ABSTRACT

Background: Morbidity and mortality associated with osteoporosis continues to be high in India due to late diagnosis. This study aims to find the difference in the levels of bone turn over markers in premenopausal and postmenopausal women, in order to assess whether these markers can be used as predictors of low bone mineral density which can develop in later life.
Methods: Study was conducted on 350 women aged 30-65 years. Women were classified into premenopausal and postmenopausal groups based on their menstrual history. Serum samples were analyzed for osteocalcin and telopeptide-C. Student's t-test and logistic regression are used for statistical confirmations.
Results: Levels of these markers (ng/ml) were found to be lower in premenopausal women (Osteocalcin = 9.0 ± 1.0; telopeptide-C = 0.270 ± 0.099) than in postmenopausal women (Osteocalcin = 9.8 ± 1.7; telopeptide-C = 0.490 ± 0.135) and this difference was found to be significant (P <0.001) for both the markers. In both the groups, telopeptide-C made significant contribution to prediction of low BMD [(Premenopausal group - odds ratio (OR) = 2.9; 95% confidence interval (95%CI) = 1.3-6.5 and postmenopausal group - OR = 9.6; 95%CI = 6.0-13.23) but osteocalcin could not (premenopausal group - OR = 0.91; 95%CI = 0.58-1.42 and postmenopausal group - OR = 0.87; 95%CI = 0.54-1.4)]. In premenopausal women increase in telopeptide-C by a unit increased chance of developing low BMD by 2.9 times while in postmenopausal women increase in telopeptide-C by a unit increased chance of developing low BMD by 9.6 times.
Conclusion: Women with higher levels of telopeptide-C need to be identified at an early stage as it provides with an early warning of the possibility of future development of osteoporosis so that preventive measures can be taken timely.

Keywords: Bone turnover markers, Bone mineral density, Osteoporosis

INTRODUCTION

Osteoporosis is a systemic skeletal disease characterized by low bone mass with a consequent increase in bone fragility and susceptibility to fracture occurring spontaneously or as a result of minor trauma. Osteoporotic fractures are a common cause of morbidity and mortality in adult Indian women.[1] Lack of estrogen accelerates bone loss. With the onset of menopause, rapid bone loss occurs which is believed to be greatest in the early postmenopausal years.[2]

Loss of bone tissue can be estimated by measuring Bone Mineral Density (BMD), but changes in BMD appear late and are relatively irreversible at this stage. Also BMD is unable to provide direct information on bone metabolism.[3] Bone Turnover Markers (BTMs) have been shown to provide valuable information for the diagnosis

and monitoring of metabolic bone disease as they reflect the whole body rates of bone resorption and bone formation.[4] BTMs thus have an advantage over measuring BMD during early stages of bone loss. They may provide a more representative index of the overall skeletal bone loss than would be obtained by measuring the rates of change in BMD at specific skeletal sites.[5]

Low BMD is a significant risk factor for osteoporotic fractures later in life.[6] Early detection of future osteoporosis is therefore 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.[7] The present study intends to evaluate the difference in the levels of the BTMs - osteocalcin and telopeptide-C in pre & postmenopausal women, in order to assess whether these markers can be used as predictors of low BMD, for early detection of osteoporosis which can develop in later life.

METHODS

This was a cross-sectional study conducted on women aged 30-65 years of urban kolar region of Bhopal visiting J.K. hospital as an attendant. Assuming prevalence of osteoporosis as 33% (WHO) and absolute precision of 5% with 95% confidence, the required sample size was estimated to be 350. 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.

Details on educational level, income, occupation, diet, exercising schedule; and medical, obstetrical, menstrual, and drug history were collected using a structured questionnaire. Information on past non traumatic fracture, family history of fracture and osteoporosis was also obtained. 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 treatment with glucocorticosteroids/thyroid hormones/hormone replacement therapy; or received treatment in past and those using oral contraceptive pills were excluded from the studies.

Women in sample, were categorized into two groups - premenopausal and postmenopausal. Menopausal criteria considered was absence of menses for at least 12 months. Five milliliters of blood was drawn from each subject and collected by venipuncture using plastic disposable syringes under aseptic measures. The samples were analyzed for osteocalcin and telopeptide-C using ELISA kits.

The data obtained was analyzed using SPSS 16 software. The statistical test used was students' t-test and logistic regression. The difference between the subjects was considered significant if the P value was less than 0.05.

RESULTS

Mean values of bone turnover markers were found to be significantly (P <0.001) lower in premenopausal women than in postmenopausal women (Table 1).

Table 1: Comparison of bone turnover marker levels in premenopausal and postmenopausal women using Students-t test.

Parameters (ng/ml)	Mean ± SD		T-score	P value
	Pre-menopausal (n=180)	Post-menopausal (n=170)		
Osteocalcin	9.0 ± 1.0	9.8 ± 1.7	5.5	<0.001
Telopeptide-C	0.270 ± 0.099	0.490 ± 0.135	17.3	<0.001

A logistic regression analysis was conducted to predict likelihood of developing low BMD using bone markers - osteocalcin and telopeptide-C as predictors.

In premenopausal women Nagelkerke's R2 of 0.769 indicated a strong relationship of 76.9% between predictors and the prediction. The Wald criterion demonstrated that telopeptide-C (P <0.001) made a significant contribution to prediction but osteocalcin (P >0.05) could not. Increase in telopeptide–C by a unit increases chance of developing low BMD by 2.9 times.

In postmenopausal women Nagelkerke's R^2 of 0.688 indicated a strong relationship of 68.8% between predictors and the prediction. The Wald criterion demonstrated that telopeptide-C (P <0.001) made a significant contribution to prediction but osteocalcin (P >0.05) could not. Increase in telopeptide-C by a unit increases chance of developing low BMD by 9.6 times (Table 2).

Table 2: Prediction of low bone mineral density in premenopausal and postmenopausal women using bone markers.

Bone markers	Premenopausal		Postmenopausal	
	Odds ratio (95% CI)	Sig.	Odds ratio (95% CI)	Sig.
Osteocalcin	0.91 (0.58, 1.42)	NS	0.87 (0.54, 1.4)	NS
Telopeptide-C	2.9 (1.3, 6.5)	<0.001	9.6 (6.0, 13.23)	<0.001

DISCUSSION

Telopeptide-C a marker of bone resorption is found to be significantly elevated in the postmenopausal women as compared to premenopausal women.[8,9] Elevated levels of telopeptide-C reflects the increased level of osteoclastic activity in the bone-remodelling process.[10] Accelerated

osteoclastic activity increases bone turnover and is associated with low bone mass in both pre and postmenopausal women.[11]

Osteocalcin a marker of bone formation is found to be significantly elevated in the postmenopausal women as compared to premenopausal women. Elevated levels of osteocalcin are seen with increased bone remodeling and bone loss.[12] Osteocalcin helps in mineralization of bone as it has a high affinity for calcium and promote absorption to hydroxyapatite in the bone matrix. In osteoporotic women, deficiency of calcium may lead to lowering of formation of hydroxyapatite crystals. Thus, in the state of decreased rate of bone mineralization, free osteocalcin may be available for circulation in the blood, leading to increased concentration of osteocalcin in the serum of postmenopausal women.[13]

In both the groups telopeptide-C made a significant contribution to prediction of low BMD but osteocalcin could not. Osteocalcin is a later marker of osteoblastic activity and is a less responsive indicator.[14] In premenopausal women increase in telopeptide-C by a unit increased chance of developing low BMD by 2.9 times while in postmenopausal women this chance was found to be 9.6 times. Declining ovarian function before menopause is accompanied by reduction in bone mass and altered calcium metabolism.[15] Postmenopausal women have two times more chance of developing low BMD as compared to premenopausal women.[16-18] An increased risk of low BMD is associated with age and menopausal status.[18,19]

CONCLUSIONS

Bone turnover marker telopeptide-C can be used as predictor of low BMD, for early detection of osteoporosis which can develop in later life. Thus preventive measures can be taken timely to reduce morbidity and mortality associated with osteoporosis.

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