

## Bone Density and Biochemical Markers of Bone Turnover in Premenopausal Women and Postmenopausal Women

Dr.Sujatha.V<sup>1</sup>,Dr.Revathi.M<sup>2</sup>, Dr. Helena Rajakumari.J<sup>3</sup>, Dr.Sadana.A<sup>4</sup>,  
Dr.RadhikaRani.KC<sup>5</sup>

<sup>1</sup>Associate Professor,Department Of Physiology, Sri Venkateswara Medical College. Tirupati-A.P, India.

<sup>2</sup>Assistant Professor, Department Of Physiology, Sri Venkateswara Medical College. Tirupati-A.P, India.

<sup>3</sup>Assistant Professor,Department Of Biochemistry, Sri Venkateswara Medical College,Tirupati-A.P, India.

<sup>4</sup>Assistant Professor,Department Of Ophthalmology, Sri Venkateswara Medical College,Tirupati-A.P, India.

<sup>5</sup>Associate Professor, Department Of Pharmacology, Sri Venkateswara Medical College. Tirupati-A.P, India.

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**Abstract:** Osteoporosis is a metabolic disorder of bone that is characterized by low bone mineral density and deterioration of micro-architecture of the bone tissue leading to increased skeletal fragility and increased fracture risk. The increased risk of osteoporosis in postmenopausal women is explained by biochemical markers of bone turnover and bone mineral density which help in early identification of women who are at increased risk of fractures. The objective of the study was to analyze biochemical markers of bone turnover and bone mineral density measurements by Bone densitometer (using T-score) among postmenopausal women in comparison to premenopausal women.

A cross sectional prospective study was carried, including 40 healthy premenopausal women of 25-45 years age and 40 healthy postmenopausal women of 46-65 years age. Biochemical markers of bone turnover (Serum calcium, Phosphorus, Alkaline phosphatase) and bone mineral density were assessed among all the participants. An unpaired student T-test was used to test differences between groups.

Bone formation markers, total calcium, phosphorus were significantly decreased ( $p < 0.001$ ), serum alkaline phosphatase was significantly increased ( $p < 0.001$ ) in postmenopausal women when compared to premenopausal women. Bone mineral density was significantly decreased in postmenopausal women than premenopausal women.

This study suggests simple common biochemical markers of bone turnover and bone mineral density measurement can be used to assess the osteoporosis in postmenopausal women. We recommend that postmenopausal women should be screened for osteoporotic fracture risk which might be an important strategy in the management of postmenopausal osteoporotic fracture risk.

**Keywords:** Postmenopausal women, Osteoporosis, Total Calcium, Total alkaline phosphatase, Bone mineral density.

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### I. Introduction

The word menopause is derived from the two Greek words meno (month) and pause (to stop). Clinically the menopause is recognized to have occurred when menstruation has ceased for twelve months [ 1 ].

The word menopause means permanent cessation of menstruation due to loss of ovarian follicular activity leading to reduced ovarian hormone secretion [ 2 ]. Postmenopausal women are necessarily estrogen deficient [ 1 ].

Osteoporosis is a metabolic disorder of bone characterized by low bone mineral density and deterioration micro architecture of the bone tissue leading to increased skeletal fragility and increased fracture risk. Osteoporosis is most common in women after menopause [ 3 ].

Menopause is associated with an imbalance in bone metabolism which is due to increased osteoclastic resorption and decreased osteoblastic bone formation and the first five to ten years after menopause is the period of higher bone turnover and bone loss [ 4 ].

Approximately 35 % of postmenopausal women lose significant amounts of bone mineral during this period and are higher risk for osteoporotic fractures [ 5 ]. This silently progressing metabolic bone disease is widely prevalent in India, and osteoporotic fractures are a common cause of morbidity and mortality in adult Indian men and women [ 6 ].

According to National Health and Nutrition Survey (NHANES III), an estimated 14 million American women over age 50 years are affected by low density at the hip. The prevalence of osteoporosis increases with age for all sites, and by World Health Organization (WHO) definition, up to 70% of women over the age 80 years have osteoporosis [ 7 ].

Postmenopausal osteoporosis is a very common problem leading to increased risk of fractures [ 8 ]. Approximately 70% fractures in women aged more than 45 years being due to osteoporosis most common being hip fractures. [ 9 ]. Recent studies showed that Indians have lower bone mineral density than European counterparts [3 ]. Experts groups peg the number of osteoporosis patients in India at approximately 26 million (2003 figure), with the numbers projected to increase to 36 million by 2013 [ 10 ].

Aim of present study is to evaluate the risk of accelerated bone mass loss by assessing bone density and biochemical parameters include serum calcium, serum phosphorus and serum alkaline phosphatase. Studies have shown that high bone turnover is associated with low bone mass and increased risk of fractures. Biochemical markers of bone turnover have been shown to provide valuable information for the diagnosis and monitoring of metabolic bone disease [ 11 ].

There is sufficient evidence to state that the risk of osteoporosis and fracture increases with age and after menopause that the bone density measurements accurately predict the risk for fractures in the short term, and that treating asymptomatic women with osteoporosis reduces their risk for fracture [ 12 ].

Measurements of bone mineral density by bone densitometer is the best available method to conform or rule out diagnosis of osteoporosis by WHO criteria depending on T-score and Z-score [ 13 ].

The purpose of this study was to evaluate risk of accelerated bone density and biochemical parameters such as serum calcium, serum phosphorus, alkaline phosphatase in postmenopausal women in comparison to premenopausal women.

## **II. Materials And Methods**

We performed a cross sectional study of 80 healthy premenopausal and postmenopausal women at Department of Physiology and Biochemistry, Sri Venkateswara Medical College, Tirupati.

The study was carried after obtaining permission by institutional ethics committee and informed consent was obtained from each participant in the study. The study Group consists of 40 healthy premenopausal women (Group I) in the age group of 25-45 years considered as control group and 40 healthy postmenopausal women (Group II) in the age group of 46-65 years.

Women associated with smoking, alcoholism, subjects with hepatic diseases, renal disorders, diabetes mellitus, cushings syndrome, autoimmune diseases such as rheumatoid arthritis, women who had undergone hysterectomy, who were on hormone replacement therapy who were taking calcium or Vit -D preparations were excluded.

The menopausal status was determined on the basis of clinical history, symptoms like cessation of menstrual cycles, hot flushes and irritability. Height and weight were measured. Body mass Index ( BMI ) was calculated by using the formula weight kg/height cm<sup>2</sup> [ 14 ].

Blood samples were drawn into test tubes containing no anticoagulant. Blood specimens were centrifuged for 15 minutes at 3000 rpm and analyzed for serum total calcium, phosphorus and alkaline phosphatase. Estimation of total serum calcium was done by ortho-cresolphthalein complexone (OCPC) method, phosphorus by modified metol method, alkaline phosphatase by kinetic method. The bone mineral density was measured by Achilles ultrasound bone densitometer.

Bone quantitative ultrasound is a relatively safe, inexpensive, does not involve ionizing radiation, portable and non invasive technique for the assessment of bone mineral density, particularly suitable for use in screening programmes [15 ,16 ]. The results of BMD were analyzed on the basis of T-scores according to WHO criteria (Table-1) [ 17 ].

**Table-1 WHO criteria for assessing disease severity**

S.No	Diagnostic Classification	T-score
1	Normal	>-1.0
2	Osteopenia	-1.0 to -2.5
3	Osteoporosis	<= - 2.5
4	Severe Osteoporosis	< -2.5 with fracture

## **III. Statistical Analysis**

The Data obtained was analyzed and the differences in the mean of various parameters were compared using students T-test. Statistical analysis was performed using software SPSS windows.

**IV. Results**

**Table-II comparison of Biochemical markers of bone turnover**

S.No	Parameters Mean ± S.D.	Premenopausal n=40	Postmenopausal n=40	P-value
1	Age	32.44 ± 6.09	56.88± 7.91	< 0.001
2	BMI	27.63±5.16	26.28±4.57	P>0.05
3	Serum calcium mg/dl	10.2±0.82	8.2±1.02	<0.001
4	Serum Phosphorus mg/dl	3.8 ± 0.41	2.2±0.24	<0.001
5	Serum alkaline phosphatase µ kat/l	2.15 ±0.57	3.24±1.00	<0.001

The results of our study showed that age was significantly increased in postmenopausal women (Group II) when compared to premenopausal women (Group I or controls). There were no significant differences in BMI between two groups. There was a significant decrease in serum total calcium in postmenopausal women (P<0.001), a significant decrease in serum phosphorus in postmenopausal women (P<0.001) and significant increase in serum alkaline phosphatase (P<0.001) in postmenopausal women when compared to premenopausal women.

**Table III Number and percentage of premenopausal and postmenopausal women having normal bone mineral density, osteopenia and osteoporosis**

**Table III**

S.No	Bonemineral density T-score	Premenopausal women n=40	Postmenopausal women n=40
1	Normal >-1.0	25 (62.5%)	4 (10%)
2	Osteopenic -1.0 to -2.5	14 (35%)	20 (50%)
3	Osteoporosis <= -2.5	1 (2.5%)	16 (40%)

**Table IV: Bone mineral density in premenopausal women and postmenopausal women**

S.No	Parameter	Premenopausal Women n=40	Postmenopausal Women n=40
1	T-score	-1.32 + 0.70	-2.09 ±0.93

**Table 2 & 3**

Our study showed that out of 40 postmenopausal subjects, 10% (n=4) were normal, 50% (n=20) were osteopenic and 40% (n=16) were osteoporotic. In postmenopausal women BMD (T-score) had significant negative correlation with increasing age.

**V. Discussion**

Menopause is known to be associated with numerous physiological and biochemical changes affecting bone mineral metabolism. Biochemical parameters can give an idea as to the rates of bone formation and resorption. High rate of bone turnover correlates with low bone mass [ 18 ].

The prevalence of osteoporosis increases with age and common in postmenopausal women and by World Health Organization (WHO) definition, up to 70% of women over the age of 80 years have osteoporosis. [ 19 ].

The outcome of our study showed that the mean age in postmenopausal women (Group II) was 56.88 and 32.44 in premenopausal women which is statistically significant. Prevalence of osteoporosis increases with age. Mean BMI in postmenopausal women was 26.28 and 27.63 in premenopausal women. There were no significance differences in BMI between two groups.

Literature says that a low BMI is one of the risk factors for increased bone turnover. However, we could not find such a correlation in present study.

In our study the mean serum calcium in postmenopausal women was 8.2 mg/dl and 10.2 mg/dl in premenopausal women which is statistically significant and mean phosphorus in postmenopausal women was 2.2 mg/dl and 3.8 mg/dl in premenopausal women which is statistically significant.

Mean serum alkaline phosphatase in postmenopausal women was 3.24 µ kat/L and 2.15 µ kat /L in premenopausal women. Bone turnover increases to high levels in women soon after menopause [ 20 ].

In women the major causes of bone loss are estrogen deficiency after the menopausal and age related processes [ 21 ]

In addition estrogen deficiency may induce calcium loss by indirect effects on extra skeletal calcium homeostasis [ 22 ]. Serum alkaline phosphatase activity is the most commonly used marker of bone formation. A moderate increase in alkaline phosphatase (ALP) indicates mineralization defect in the elderly patients [ 23 ]. At the menopause the rate of bone demineralization increases [ 24 ].

Bone density is one of the major predictors of osteoporotic fractures in the elderly. In our study out of 40 postmenopausal subjects 10% (n=4) were normal, 50% (n=20) were osteopenic and 40% (n=16) were osteoporotic and in premenopausal women 62.5% (n=25) were normal, 35% (n=14) were osteopenic, 2.5% (n=1) was osteoporotic.

The mean T score in postmenopausal women was -2.09 and -1.32 in premenopausal women. In postmenopausal women BMD (T-score) had a significant correlation with increasing age. There were significant differences in T-score values between premenopausal and postmenopausal subjects (Table 4).

In Bone density is one of the major predictors of osteoporotic fractures in the elderly [ 25 ].

Bone mineral density (BMD) is the most readily available measurement that correlates strongly with bone fragility [ 26 ]. BMD is the major risk factor for osteoporotic fracture. An increased risk of low BMD associated with age and menopausal status.

Our study correlates with the other studies reporting lower bone mineral density values that are continued to decrease after the onset of menopause, Nuti R and Martini G et al [ 27 ].

Our study correlates with the previous studies. O Madhuri V and Keerthi reddy M et al 2010, Granney A et al.

## VI. Conclusion

In postmenopausal women with osteoporosis biochemical markers of bone formation and bone resorption increases, because of more osteoclastic activity.

In the present study postmenopausal women showed significant decrease in serum calcium, serum phosphorus with a significant increase in serum alkaline phosphatase values.

Bone mineral density in postmenopausal women was decreased and indicates osteoporotic risk.

We conclude that biochemical markers of bone turnover and bone mineral density are valuable tools in detecting osteoporosis in postmenopausal women.

We recommend that postmenopausal women should be screened for osteoporotic fracture risks which might be an important strategy in the management of postmenopausal osteoporotic fracture risk.

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