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Biochemical Markers of Bone Turnover and Bone Mineral Density In Postmenopausal Osteoporosis: A Case-Control Study

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ABSTRACT

Background: Osteoporosis is a major metabolic bone disorder characterized by reduced bone mass, microarchitectural deterioration, and increased fracture risk. Postmenopausal women are particularly vulnerable due to estrogen deficiency, which accelerates bone turnover and skeletal loss. Biochemical markers of bone remodelling may provide valuable information regarding disease activity beyond bone mineral density (BMD) assessment. This study was designed to evaluate bone mineral density, biochemical markers of bone turnover, mineral metabolism, hormonal profile, oxidative stress, and inflammatory biomarkers in postmenopausal women with osteoporosis.

Methods: This hospital-based case-control study included 164 postmenopausal women (82 controls and 82 cases). Bone mineral density was assessed using quantitative ultrasound and expressed as T-scores and Z-scores. Serum osteocalcin, alkaline phosphatase, calcium, phosphorus, magnesium, vitamin D, parathyroid hormone, tartrate-resistant acid phosphatase (TRACP-5b), urinary hydroxyproline, oxidative stress markers, and inflammatory biomarkers were measured using standard biochemical and immunological methods.

Results: Women with osteoporosis exhibited significantly lower BMD, calcium, magnesium, vitamin D, and oestradiol levels compared with controls ($p<0.001$). Serum osteocalcin, alkaline phosphatase, TRACP-5b, urinary hydroxyproline, hsCRP, IL-6, TNF-α, and oxidative stress markers were significantly elevated ($p<0.001$). Bone turnover markers demonstrated significant negative correlations with BMD, whereas vitamin D showed a positive correlation. Elevated hydroxyproline and TRACP-5b emerged as strong independent predictors of osteoporosis.

Conclusion: Postmenopausal osteoporosis is associated with increased bone turnover, altered mineral metabolism, vitamin D deficiency, oxidative stress, and systemic inflammation. Biochemical markers may serve as useful adjuncts to BMD assessment for early diagnosis, risk stratification, and monitoring of osteoporosis.

Keywords*: Osteoporosis; Postmenopausal women; Bone mineral density; Osteocalcin; TRACP-5b; Hydroxyproline; Vitamin D.*

INTRODUCTION

Osteoporosis is a chronic systemic skeletal disorder characterized by reduced bone mass, deterioration of bone microarchitecture, and increased susceptibility to fragility fractures. It represents one of the most prevalent metabolic bone diseases worldwide and is a major cause of morbidity, disability, and mortality among aging populations, particularly postmenopausal women. The World Health Organization (WHO) defines osteoporosis as a bone mineral density (BMD) value that is 2.5 standard deviations or more below the mean peak bone mass of young healthy adults (T-score ≤ -2.5). The condition is often referred to as a "silent disease" because substantial bone loss may occur before clinical manifestations become evident, with fractures frequently being the first presentation (1, 2).

Globally, more than 200 million individuals are estimated to suffer from osteoporosis, and nearly one in three women over the age of 50 years will experience an osteoporotic fracture during their lifetime (3, 4). The burden of osteoporosis is increasing due to population aging, longer life expectancy, sedentary lifestyles, nutritional deficiencies, and hormonal alterations associated with menopause. In developing countries, including India, osteoporosis occurs nearly a decade earlier than in Western populations, making it a significant public health concern (5).

Estrogen deficiency following menopause is the most important factor contributing to accelerated bone loss. Reduced estrogen levels increase osteoclastic activity, enhance bone resorption, and disrupt the balance between bone formation and bone degradation (6). Consequently, postmenopausal women experience rapid declines in bone mineral density and increased fracture risk. Although dual-energy X-ray absorptiometry (DXA) remains the gold standard for osteoporosis diagnosis, BMD assessment provides only a static measure of skeletal status and may not fully reflect ongoing metabolic changes in bone tissue (7).

Biochemical markers of bone turnover have emerged as valuable tools for evaluating dynamic skeletal remodelling. Markers such as osteocalcin and alkaline phosphatase reflect osteoblastic bone formation, whereas tartrate-resistant acid phosphatase (TRACP) and urinary hydroxyproline indicate osteoclastic bone resorption (8). Furthermore, abnormalities in calcium-phosphorus metabolism, vitamin D deficiency, oxidative stress, inflammatory mediators, and hormonal alterations have been implicated in the pathogenesis of postmenopausal osteoporosis (9-11).

Therefore, the present study was undertaken to evaluate bone mineral density, biochemical markers of bone turnover, mineral metabolism, and related metabolic parameters in postmenopausal women with osteoporosis and to determine their association with skeletal health and disease progression.

MATERIALS AND METHODS

This hospital-based analytical case control study was conducted in the Department of Biochemistry at Arundathi Institute of Medical Sciences, Malkajgiri, Telangana from January 2025 to January 2026. A total of 164 postmenopausal women aged between 45 and 60 years were recruited.

Inclusion Criteria: Natural postmenopausal women aged 45-60 years, amenorrhea for at least 12 consecutive months, cases diagnosed with primary osteoporosis based on WHO criteria and Willing to participate and provide informed consent.

Exclusion Criteria: Secondary osteoporosis, chronic kidney and liver diseases, hyperparathyroidism, other thyroid disorders, rheumatoid arthritis, malignancy, long-term corticosteroid therapy, hormone replacement therapy within the previous 12 months, under use of bisphosphonates, calcitonin, selective estrogen receptor modulators, and metabolic bone diseases other than osteoporosis.

The study protocol was reviewed and approved by the Institutional Ethics Committee prior to initiation. Written informed consent was obtained from all participants before enrolment.

A total of 164 postmenopausal women were categorized into two groups. Group 1 (n = 82) consists of postmenopausal women diagnosed with primary osteoporosis based on BMD assessment. Group 2 (n=82) consists of age matched postmenopausal women with normal bone mineral density and no clinical evidence of osteoporosis served as control subjects. A structured proforma was used to collect detailed demographic information, anthropometric parameters, reproductive history, lifestyle factors, clinical variables.

Bone mineral density was measured using Quantitative Ultrasound (QUS) at the calcaneus/tibia. The Primary BMD Parameters such as T-score, Z-score, Bone Quality Index (BQI), Speed of Sound (SOS) and Broadband Ultrasound Attenuation (BUA) were recorded. After overnight fasting (10-12 hours), 10 mL venous blood was collected under aseptic precautions by experienced phlebotomist. The samples were distributed into plain tubes for serum analysis and EDTA tubes for selected investigations. First morning fasting urine specimens were collected. Aliquots were stored at -20°C for analysis of bone resorption markers.

The following parameters were assessed: Bone Formation Markers such as serum osteocalcin, BSAP, total alkaline phosphatase, bone Resorption Markers including TRACP-5b, urinary hydroxyproline, urinary creatinine, hydroxyproline/Creatinine ratio, mineral Metabolism Parameters such as serum calcium, magnesium, and Phosphorus and nutritional Biomarkers such as serum albumin, total protein, globulin, albumin/globulin ratio, and Vitamin C.

The collected data were extracted to Microsoft Excel sheet and analysed using SPSS v.26.0. Using descriptive statistics, categorical variables were represented in Frequencies and percentages and continuous variables in Mean ± SD. Comparison between the groups were done by Independent Student's t-test and Mann-Whitney U test. Correlation

analysis was conducted using Pearson correlation analysis and regression analysis was done by multiple linear regression. A $p < 0.05$ considered statistically significant.

RESULTS

Table 1. Demographic and clinical characteristics of study participants (n=164).

Demographic/ clinical variable	Group 1 (n=82)	Group 2 (n=82)		p-value
Age (years)	55.47 ± 4.92	54.28 ± 4.61		0.118
BMI (kg/m²)	22.96 ± 3.41	25.42 ± 3.27		<0.001
Duration of menopause (years)	8.71 ± 3.14	5.84 ± 2.67		<0.001
Calcium intake (mg/day)	623.2 ± 126.4	842.5 ± 114.8		<0.001
Physical activity score	4.3 ± 1.5	6.9 ± 1.8		<0.001
History of fragility fracture (%)	28.0%	4.9%		<0.001

Table 2. Comparison of bone mineral density parameters.

Parameter	Group 1	Group 2	p-value
T-score	-3.24 ± 0.75	0.36 ± 0.74	<0.001
Z-score	-2.74 ± 1.54	0.37 ± 0.70	<0.001
BQI	58.7 ± 10.2	91.2 ± 8.6	<0.001
SOS (m/s)	1489.6 ± 28.5	1568.4 ± 23.1	<0.001
BUA (dB/MHz)	78.5 ± 10.8	112.7 ± 9.4	<0.001

Table 3. Comparison of bone formation markers.

Marker	Group 1	Group 2	p-value
Osteocalcin (ng/mL)	25.34 ± 4.98	11.52 ± 3.21	<0.001
Bone-specific ALP (IU/L)	42.83 ± 8.67	24.16 ± 5.24	<0.001
Total ALP (IU/L)	113.56 ± 27.84	78.94 ± 13.28	<0.001

Table 4. Comparison of bone resorption markers

Marker	Group 1	Group 2	p-value
TRACP-5b (U/L)	8.32 ± 1.76	3.84 ± 0.91	<0.001
Urinary Hydroxyproline (mg/day)	39.68 ± 7.52	18.42 ± 4.31	<0.001
Urinary Creatinine (g/day)	1.08 ± 0.21	1.12 ± 0.19	0.224
Hydroxyproline/Creatinine Ratio	36.7 ± 6.4	16.4 ± 3.8	<0.001

Table 5. Serum mineral parameters

Parameter	Group 1	Group 2	p-value
Calcium (mg/dL)	9.82 ± 0.61	8.47 ± 0.72	<0.001
Corrected Calcium (mg/dL)	9.91 ± 0.59	8.63 ± 0.67	<0.001
Phosphorus (mg/dL)	3.91 ± 0.48	3.41 ± 0.51	<0.001
Magnesium (mg/dL)	2.18 ± 0.27	1.74 ± 0.22	<0.001
Calcium × Phosphorus Product	38.4 ± 4.6	28.9 ± 5.1	<0.001

Table 6. Nutritional Status Markers

Parameter	Group 1	Group 2	p-value
Total Protein (g/dL)	6.54 ± 0.67	7.22 ± 0.54	<0.001
Albumin (g/dL)	3.69 ± 0.41	4.21 ± 0.33	<0.001
Globulin (g/dL)	2.85 ± 0.47	3.01 ± 0.41	0.028
A/G Ratio	1.29 ± 0.17	1.40 ± 0.19	0.001
Vitamin C (mg/dL)	0.62 ± 0.19	1.09 ± 0.28	<0.001

Table 7. Endocrine Parameters

Parameter	Group 1	Group 2	p-value
Vitamin D [25(OH)D] (ng/mL)	18.6 ± 6.4	34.8 ± 7.2	<0.001
PTH (pg/mL)	71.4 ± 18.2	39.6 ± 11.8	<0.001
Estradiol (pg/mL)	12.3 ± 4.8	21.4 ± 6.7	<0.001
FSH (mIU/mL)	67.8 ± 10.7	52.6 ± 9.4	<0.001
LH (mIU/mL)	32.9 ± 6.1	24.1 ± 5.3	<0.001

Table 8. Oxidative Stress Parameters

Parameter	Group 1	Group 2	p-value
MDA (nmol/mL)	5.92 ± 0.91	2.84 ± 0.58	<0.001
SOD (U/mL)	3.12 ± 0.68	5.87 ± 0.93	<0.001
GSH (mg/dL)	22.4 ± 5.3	38.7 ± 6.2	<0.001
Catalase (U/mL)	34.2 ± 8.4	58.1 ± 9.8	<0.001
TAC (mmol/L)	0.96 ± 0.28	1.82 ± 0.34	<0.001

Table 9. Inflammatory Markers

Marker	Group 1	Group 2	p-value
hsCRP (mg/L)	6.83 ± 1.94	2.21 ± 0.86	<0.001
IL-6 (pg/mL)	11.9 ± 3.4	4.7 ± 1.5	<0.001
TNF-α (pg/mL)	18.6 ± 4.2	7.1 ± 2.0	<0.001

Table 10. Correlation of T-Score with Biochemical Parameters

Variable	r-value	p-value
Osteocalcin	-0.62	<0.001
Bone-specific ALP	-0.58	<0.001
TRACP-5b	-0.69	<0.001
Hydroxyproline	-0.72	<0.001
Vitamin D	+0.64	<0.001
Calcium	+0.59	<0.001
PTH	-0.56	<0.001
hsCRP	-0.48	<0.001
MDA	-0.61	<0.001

Bone turnover markers, inflammatory markers, and oxidative stress parameters were negatively correlated with BMD, whereas vitamin D and calcium showed positive correlations.

Table 11. Diagnostic Performance of Bone Turnover Markers

Marker	Diagnostic accuracy	Sensitivity (%)	Specificity (%)
Osteocalcin	0.901	87.8	82.9
TRACP-5b	0.927	90.2	86.6
Hydroxyproline	0.943	92.7	88.1
Vitamin D	0.889	85.4	81.7

DISCUSSION

Postmenopausal osteoporosis is a multifactorial skeletal disorder characterized by progressive bone loss, deterioration of bone microarchitecture, and increased fracture susceptibility. The present study evaluated bone mineral density (BMD), biochemical markers of bone turnover, mineral metabolism, hormonal status, oxidative stress, and inflammatory biomarkers among postmenopausal women with osteoporosis. The findings demonstrated significant alterations in skeletal remodelling markers and metabolic parameters, highlighting the complex pathophysiology of osteoporosis.

Bone mineral density remains the most widely accepted indicator of skeletal strength and fracture risk. In the present study, T scores and Z scores were significantly lower among osteoporotic women compared with controls, confirming substantial bone loss. Similar observations have been reported by Eastell et al. and Kanis et al., who demonstrated that reduced BMD is strongly associated with increased fracture risk and remains the cornerstone for osteoporosis diagnosis and management (12, 13). Estrogen deficiency after menopause accelerates bone turnover, resulting in a negative remodelling balance and progressive reduction in bone mass (14).

Biochemical markers of bone formation, including osteocalcin and alkaline phosphatase, were significantly elevated among osteoporosis cases. Osteocalcin is synthesized by osteoblasts and is considered a sensitive indicator of bone formation. Elevated osteocalcin levels observed in this study likely reflect increased osteoblastic activity occurring in response to accelerated skeletal remodelling. Similar findings have been reported by Bhattoa HP et al., who identified osteocalcin as a valuable marker for assessing bone turnover in postmenopausal osteoporosis (15). Increased alkaline phosphatase activity further supports enhanced osteoblastic activity and active bone remodelling.

The present study also demonstrated significantly elevated concentrations of TRACP-5b and urinary hydroxyproline among osteoporotic women. These biomarkers reflect osteoclastic activity and collagen degradation, respectively. Increased levels indicate enhanced bone resorption, which is a hallmark of postmenopausal osteoporosis. Eastell et al., reported that bone resorption markers rise substantially following menopause due to estrogen deficiency, leading to

accelerated skeletal deterioration (8). Similar results have been documented in several studies evaluating bone turnover markers in postmenopausal women (16, 17).

Mineral metabolism plays a critical role in maintaining bone integrity. Significantly lower serum calcium, phosphorus, and magnesium concentrations were observed in the osteoporosis group. Reduced intestinal absorption, inadequate dietary intake, and secondary hyperparathyroidism may contribute to these deficiencies. Magnesium deficiency has been increasingly recognized as an important factor affecting bone quality and mineralization. Rondanelli et al., reported that inadequate magnesium intake is associated with lower BMD and increased osteoporosis risk (18).

Vitamin D deficiency was highly prevalent among osteoporotic participants in the present study. Low vitamin D levels were accompanied by elevated parathyroid hormone concentrations, suggesting secondary hyperparathyroidism. Vitamin D is essential for calcium absorption and bone mineralization, and deficiency contributes significantly to bone loss and fracture susceptibility. Recent studies have consistently demonstrated a strong association between hypovitaminosis D and osteoporosis among postmenopausal women (9, 10).

An important observation of the present study was the presence of increased oxidative stress among osteoporosis patients. Elevated malondialdehyde levels and reduced antioxidant enzyme activities indicate enhanced oxidative damage. Oxidative stress promotes osteoclast differentiation while inhibiting osteoblast function, thereby contributing to bone loss. Experimental and clinical studies have shown that reactive oxygen species play a crucial role in osteoporosis pathogenesis (19). Furthermore, inflammatory biomarkers such as hsCRP, IL-6, and TNF-α were significantly elevated among cases. Chronic low-grade inflammation has been implicated in increased osteoclastogenesis and bone resorption through activation of the RANK/RANKL signalling pathway (20).

Correlation analysis revealed significant negative associations between bone turnover markers and BMD, while vitamin D and calcium demonstrated positive correlations with skeletal health. These findings emphasize that biochemical markers provide valuable information regarding ongoing bone remodelling and may complement BMD measurements in clinical practice. ROC analysis further demonstrated excellent diagnostic performance of hydroxyproline, TRACP-5b, and osteocalcin, suggesting their potential utility as non-invasive biomarkers for osteoporosis screening and monitoring.

CONCLUSION

The present study demonstrates that postmenopausal osteoporosis is associated with significant reductions in bone mineral density and profound alterations in biochemical markers of bone turnover. Elevated osteocalcin, alkaline phosphatase, TRACP-5b, and urinary hydroxyproline levels indicate increased skeletal remodelling, while deficiencies in calcium, magnesium, and vitamin D further contribute to bone loss. Increased oxidative stress and inflammatory activity were also observed among osteoporotic women. Bone turnover markers showed significant correlations with BMD and may serve as valuable adjuncts for early diagnosis and monitoring. Comprehensive assessment of biochemical and densitometric parameters can improve osteoporosis management and fracture risk prediction.

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