www.jmscr.igmpublication.org Impact Factor 3.79
ISSN (e)-2347-176x

IGM Publication Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Bone Turnover Markers in Post Menopausal Osteoporosis- A Case Control Study

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ABSTRACT

Osteoporosis is a major health problem worldwide and is projected to increase exponentially due to aging. In post-menopausal women rapid bone loss occurs due to hormonal factors leading to enhanced bone fragility and consequent increased risk of fractures. Measurement of serum and urinary bone turnover markers provide valuable information for diagnosis and monitoring of metabolic bone disease. Bone resorption marker urinary hydroxyproline and bone formation markers serum and urinary calcium, phosphorous were analysed to assess the skeletal turnover in the present study. Significantly increased excretion of hydroxyproline and calcium in urine, significant decrease in serum calcium and increase in serum phosphorous was observed in post-menopausal women when compared to controls. Hence this study suggests that simple, common bio-chemical markers can be used to assess the bone turnover and the risk of developing osteoporosis and fractures in postmenopausal women.

Keywords- *Post-menopausal osteoporosis, Bone turnover markers, Urinary Hydroxyproline, Calcium, Phosphorous.*

Introduction

Osteoporosis is a disease that weakens bone and leads to progressive loss of bone mass that occurs in elderly of both sexes but it is more pronounced in postmenopausal women[1] . Osteoporosis is used to define any degree of skeletal fragility, sufficient to increase the risk of fracture[2]. Postmenopausal osteoporosis is a metabolic disease characterised by reduction of bone mass with normal mineral content of the remaining bone tissue. As a women makes the natural transition through Menopause, Ovaries stop producing Oestrogen leading to an increasing number of health risks including osteoporosis[3].The prevalence of Osteoporosis increases with age by WHO definition unto 70% of the women over 80 years of age have osteoporosis[4].Bone is composed primarily of inorganic minerals calcium and phosphate and an organic matrix (Type 1 collagen). The concentration of calcium phosphate is dependent on the net effect of bone mineral deposition and resorption[5]. Calcium is the fifth most common element and an average human contains approximately 1 kg of Calcium. The skeleton contains 99% of body's calcium as extra cellular crystals [6]. Calcium salts in bone are embedded in collagen fibrils among that 13% is mainly hydroxylproline, during osteoporosis collagen fibrils are broken down and hydroxyproline is excreted in urine [7].

Until third decade of life a person normally builds more bone than they lose. During the ageing process, bone break down begins to outpace bone building, resulting gradual loss of bone mass which predisposes to Osteoporosis [8]. Estrogen deficiency at the menopause increases the rate of bone remodelling, which results in high turnover of bone loss [9]. Until recently the diagnosis of Osteoporosis was based primarily on clinical and radiological methods. Studies have shown that bone turnover is high in Osteoporosis, Markers such as urinary hydroxyproline, Serum and urinary calcium and phosphate have been found to be reliable [10].

The commonest cause of Osteoporosis being menopause, the present study was carried out by analysing these parameters to assess the bone turnover.

Materials and Methods

The study was conducted in department of Bio-chemistry and department of Orthopaedics, Sri Venkateshwara Medical College / Sri Venkateswara Ramnarayan Ruia Government General Hospital, Tirupati.

40 Postmenopausal women between 45-70 years as study group and 20 pre-menopausal women between 25-45 years as control group were included in the study.

Informed written consent was obtained from all the individuals involved in the study.

3 ml of venous blood was collected after overnight fast of 12-14 hours from each participant. Serum was separated by centrifugation at 3,000 rpm for 10 minutes and stored at - 20ºC until analysis.

24 hours urine sample was collected, PH of urine was adjusted to >2 by adding 2ml HCL and mixed thoroughly. Total volume of urine was measured and aliquots were stored at -20^{0}C until analysis.

Serum and urinary calcium was estimated spectrophotometrically by O – Cresolphthalein Complexone method [11].

Serum and urinary phosphorous was measured spectrophotometrically by the reaction to form phosphomolibdate complex [12].

Urinary hydroxyproline was analysed by Neuman and Logan method modified by A.A.Leach [13].

Results

The results were expressed as mean and standard deviation (SD). Statistical analysis was studied by using student t-test. A p-value of < 0.05 was considered to be statistically significant. The bone mineral status was assessed by estimating calcium and phosphorous in serum and 24 hours urine sample, Bone resorption markers by urinary hydroxyproline.

Table 1: Mean ± SD of various biochemical parameters in the study group and control group.

S.N	Parameter	Study group n = 40 mean ± SD	Control group n = 20 mean ± SD	p-value
1	U.Hydroxy proline mg/day	3.46± 1.09	2.62 ± 1.18	<0.05
2	S.Calcium mg/dl	8.24±0.66	9.41 ± 0.48	<0.05
3	S.Phosphorous mg/dl	3.67± 0.88	3.19 ± 0.56	<0.05
4	U.Calcium mg/day	216.05 ± 128.13	146.8 ± 46.79	<0.05
5	U.phosphorous mg/day	445.2 ± 193.3	458.85 ± 104.72	NS

The mean urinary hydroxyproline levels in the study group was 3.46± 1.09 which was significantly higher than the control group 2.62 ± 1.18 (P<0.05).

Mean serum calcium levels was 8.24± 0.66 in the study group and 9.41 ± 0.48 in the control group which was statistically significant (p<0.05).

Mean serum phosphorous in the study group was 3.67 ± 0.88 which was significantly increased than the control group 3.19 ± 0.56 (p < 0.05).

Mean urinary calcium in the study group was 216.05 ± 128.13 and in the control group was 146.8 ± 46.79. Significant increase was observed in study group (p<0.05).

Urinary phosphorous does not show statistical significance between the two groups.

Discussion

Osteoporosis is the most common problem in post-menopausal women. Decreased levels of estrogen leads to enhanced bone resorption which in turn causes loss of bone density resulting in osteoporosis. During bone loss collagen fibrils are broken down and hydroxyproline is excreted in urine. Urinary hydroxyl proline is considered as an index of bone resorption and a major determinant of bone status [3].

In the present study there was a significant increased urinary excretion of hydroxyproline in the study group compared to the control group [3, 9, 10, 14].

Serum calcium, the marker of bone formation was significantly decreased in the study group when compared to the control group [3, 8, 9].

Serum phosphorous was also significantly increased in the study group than the control group [9].

There was significant correlation of urinary calcium in the study group compared to the control group [3, 5, 6, 7, 9, 10, 15].

There was no significant difference in urinary phosphorous levels in our study.

The increased urinary excretion of calcium and phosphorous affects the quality of bone. During bone loss collagen fibrils are broken down, thus calcium and hydroxyproline are excreted in urine.

Conclusion

Our study suggests that biochemical markers such as urinary hydroxyl proline, serum calcium, serum phosphorous and urinary calcium could be used as indicators of increased bone turnover. By selecting these appropriate biochemical bone turnover markers risk of fracture can be predicted and is beneficial in the treatment of postmenopausal osteoporotic women.

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