STUDY OF BIOCHEMICAL BONE TURNOVER MARKERS IN POSTMENOPAUSAL WOMEN LEADING TO OSTEOPOROSIS

Sk.Deepthi, G.Amar Raghu Narayan and J.N.Naidu

Department of Biochemistry and Plastic surgery.
Narayana Medical College & Hospital, Nellore, India.
Corresponding Authors mail : drskdeepthi@gmai.com

ABSTRACT: Osteoporosis is the term used for diseases that cause a reduction in the mass of bone perunit volume and is one of the dreaded afflictions of ageing.

Osteoporosis increases bone fragility and susceptibility to fractures. This silently progressing metabolic bone disease is widely prevealent in India.

This study was conducted to evaluate the role of biochemical bone turnover markers in postmenopausal women to assess the risk of osteoporosis.

Study includes 70 women (40 postmenopausal, 30 premenopausal women) serum estradiol, serum alkaline phosphatase, urinary hydroxyproline were estimated in both cases and controls.

There is decrease in serum estrodiaol levels in postmenopausal women when compared to premenopausal women estrogen deficiency induces bone loss similarly ALP is highly significant $P<0.001$ in prostmenopausal women suggesting that there is high alkaline phosphate activity in postmenopausal women as a result of the inhibitory effects of estrogen on bone turnover rate which is dependent on age and body mass index.

Increased excretion of urinary hydroxyproline is due to increase in bone loss and this was a characteristic feature of immediate postmenopausal period.

Key words: ALP – Alkaline Phosphatase, UHP – Urinary Hydroxyproline

INTRODUCTION

Bone is a dynamic tissue that is remodeled constantly through out life. The arrangement of compact and cancellous bone provides strength and density suitable for mobility and protection (Harrison text book 16th edi). There are two main types of bone cells they ae osteoclasts and osteoblasts. Bone cells participate in the growth, modeling and remodeling of bone (Endres DB Tietz text book 3rd edition).

An accelerated loss of corticalbone is superimposed on age related loss around menopause (Krane SM Kolick M.F Harrison's 13th edition).

Menopause is the permanent cessation of menstruation due to loss of ovarian follicular function, which results in decreased production of estradial and other hormones. Decreased levels of estrogen leads to increased osteoclast formationl and enchanced bone resorption, which inturn leads to loss of bone density and destruction of local architecture resulting in microfractures.

Osteoporosis is the term used for diseases that cause a reduction in the mass of bone per unit volume and is one of the dreaded afflication of ageing (Carr BR, Brad Shaw K.D Harrison's 14th edition). In India experts groups peg the number of osteoporosis to increase by 36 million by 2013.

The prevalence of osteoporosis increases with age, by WHO definition upto 70% of women over the age 80 years have osteoporosis (Facts and statistics about osteoporosis 2003).

Bone biopsy is an invasive procedure hence biochemical assessment of skeletalmetabolism hold great importance. Biochemical markders reflect alteration in bone remodeling much earlier that they are apparent radiographically.

The aim of the study was to assess the clinical utility of biochemical markers of bone turnover such as serum alkaline phosphatase, urinary hydroxyproline and estradiol as in premenopausal and postmenopausald women to asses the risk of osteoporis in postmenopausal women.

MATERIALS AND METHODS

The study was conducted over 70 subjects attending out patient departments in orthopedics and gynecology department in Narayana Medical College, Nellore.

Informed consent was obtained from patients and controls.

Out of 70 subjects, 30 healthy premenopausal women volunteer (25 – 40 years) and 40 healthy postmenopausal women in the age group of 55 – 65 years were taken.

5 ml of venous blood was collected aseptically from antecubital vein in the morning after 12 hrs of overnight fasting and serum was separated by centrifugation and analyzed.

6 hrs urine was collected by instructing subjects to begin collection immediately after completion of first voiding in morning and to collect all urine into same container by adding a preservative (Hcl 5ml/L of urine) this was thoroughly mixed and a sample of 2mlf was taken for evaluation of urinary hydroxyproline. Total volume was noted and calculation wad done for 24 hrs.

Serum alkaline phsophatase was estimated by optimized standard method (Schettler G 1975)(Richmond W 1973) (Rosch Lag P 1974). Serum estradiol was estimated by immune enzymatic assay (Chinyera Adanna Opara Usoro 2007)(Beck Jensen JE, Kolleru PG 1997). Urinary hydroxy proline was estimated by modified neuman and logan method(Ashuma.such deva 2005)(Mitoma.C Smith 1959).

RESULTS

Data analysis was done using statistical method of SPSS version 11.0

Study variables were expressed in terms of mean ± standard deviation (S.D) variability across the study groups for each of the variable was assessed using non parametric test Mann whitney's test. The p value <0.05 was considered as significant.

Table –1 Comparison **of Estradiol Levels between cases (post menopausal) and Controls (pre menopausal) pg/ml**

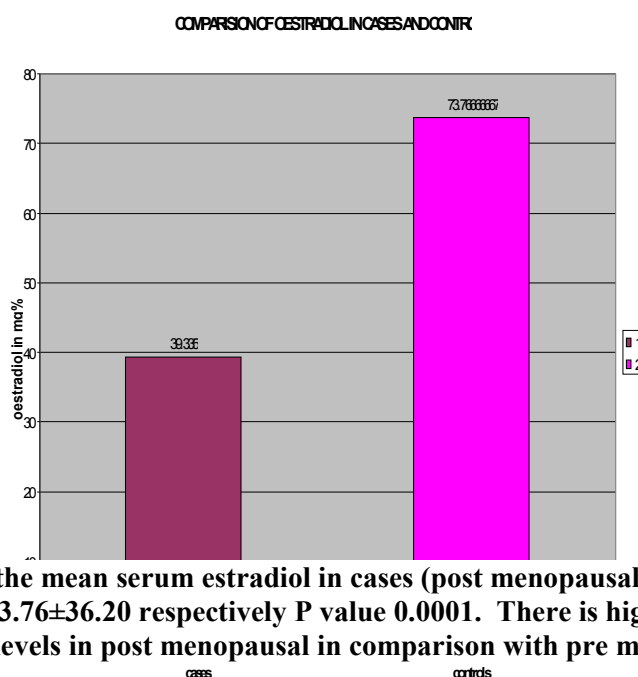| Parameters	Cases n = 40 (post mw)	Control n = 30(pre mw)	P value	T value
Oestradiol	39.33±13.36	73.76±36.20	0.0001	5.543

Figure : 1 shows the mean serum estradiol in cases (post menopausal) and controls(pre menopausal) are 39.33±13.36 and 73.76±36.20 respectively P value 0.0001. There is highly significant elevation in estradiol levels in post menopausal in comparison with pre menopausal women.

Table – 2 Comparision of Urinary Hydroxyl Proline Levels between cases (post menopausal)and Controls (pre menopausal) mg/24hrs Urine

Parameters	Cases n = 40	Control n = 30	P value	T value
UHP	104.04±28.60	60.96±8.49	0.0001	7.975

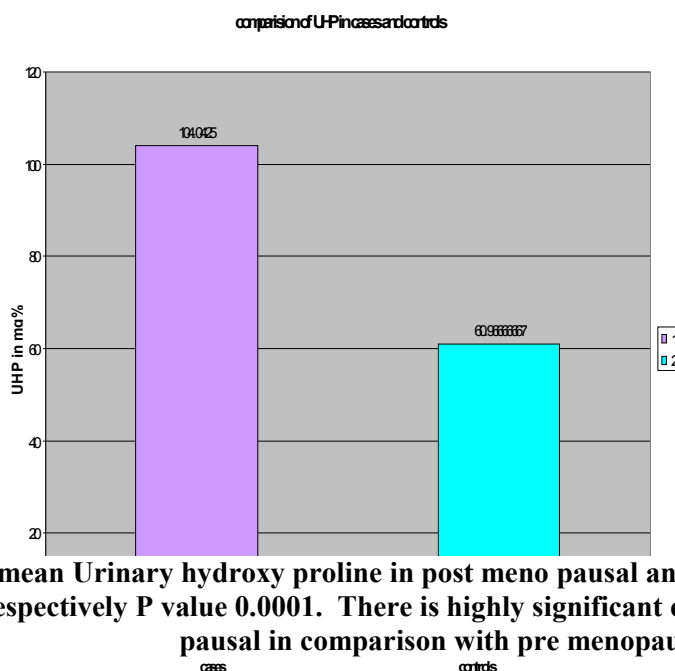comparision of UHP in cases and controls

Figure: 2 shows mean Urinary hydroxy proline in post meno pausal and pre menopausal are 104.04±28.60 and 60.96±8.49 respectively P value 0.0001. There is highly significant elevation in UHP levels in post meno pausal in comparison with pre menopausal .

Table –3:Comparision of Alkaline Phosphatase Levels between cases (post meno pausal) and Controls (pre menopausal) IU/lit

Parameters	Cases n = 40	Control n = 30	P value	T value
ALP	158.42±37.02	130.70±21.97	0.001	3.644

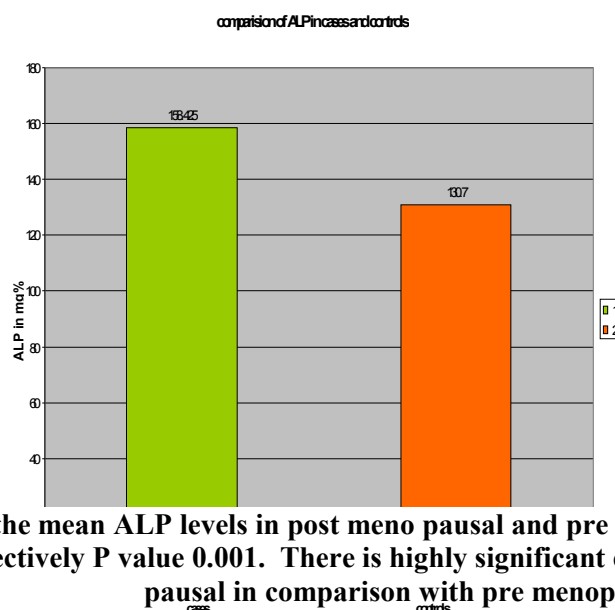comparision of ALP in cases and controls

Figure:3 shows the mean ALP levels in post meno pausal and pre menopausal are 158.42±37.02 and 130.70±21.97 respectively P value 0.001. There is highly significant elevation in ALP levels in post meno pausal in comparison with pre menopausal.

DISCUSSION

Menopause and ageing is associated with loss of approximately 50% of trabecular bone. Bone loss occurs when the balance between formation and resorption is upset and resorption is excessive resulting in a negative remodeling balance(Ashuma.Such deva 2005)(Dogan .E c.Posaci 1978). Which ultimately results in osteoporotic fractures in postmenopausal women.

Serum alkaline phosphatase is the most commonly used markers of bone formation. ALP is a ubiquitous enzyme that plays an important role in osteoid formation and mineralization.

In our study the mean value of serum ALP in post menopausal women is 158.42 ± 37.02 Iu/L and in premenopausal women is 130.70 ± 21.9 respectively. The mena value of serum ALP in postmenopausal women is higher when compared to premenopausal women(Ashuma.Such deva 2005)(Meena Verma, Sangeta panei 2005-08). It is observed that ALP levels were high in early postmenopausal women when compared to those of premenopausal women as a result of the inhibitory effects of estrogen on bone turnover ate which is dependent on age and body mass index.

Urinary hydroxyproline, the most performed measure of bone resorption, has the longest history of use(Carvo MS, Eyre Dr.1996).

In our study the mean value of excretion of hydroxyproline in cases is 104.04 ± 28.60 mg/24hrs and in controls it is 60.96 ± 8.49 respectively. The excretion of hydroxyproline was increased in postmenopausal women as compared to premenopausal women. The increase was highly significant. p value <0.001 (Aydeniz Ali 2006)(Sarrel P,M1990).

This increase excretion is due to increase in bone loss and this was a characterstic feature of the immediate postmenopausal period.

Estrogen plays an important role in growth and maturation of bone as well as in the regulationof bone turnover in adult bone. During bone growth estrogen is needed for proper closure of epiphyseal growth plates both in females and in males.

In our present study mean values serum estradioal in cases was 39.33 ± 13.36 pg/ml and in controls it was 73.76 ± 36.20 respectively which is highly significant p value <0.001.

There is decrease in serum estradiol levels in postmenopausal women when compared to premenopausal women.

Hence present study supports the view that estrogen deficiency induces bone low, highly increased bone resorption in cancellous bone leads to general bone loss and destrution of local architecture and reduced bone strength resulting in osteoporosis.

ACKNOWLEDGEMENT

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