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Effect of menopausal condition on serum estradiol levels and bone health among urban women

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Abstract
The female sex hormone, estrogen plays an important role in maintaining bone strength. Estrogen levels drop during menopause, at around the age of 45 years resulting in increased bone loss. Based on this back ground, the present study focused on estimating the changes in serum estradiol levels both in pre and postmenopausal women as well as in terms of menopausal nature as premature, early, ideal and late menopausal conditions. The findings well demonstrated that estrogen levels dropped to half of the levels of premenopausal women in postmenopausal women. The interesting point observed that simultaneously there was a decline in the levels of bone mineral density. Thus it was clear that menopause and age related bone loss were inevitable processes and hence adopting measures to improve estrogenic effect and in turn enhancing bone mass might be beneficial to restore bone health.

Keywords: Premenopause, postmenopausal women, Serum Estradiol, Bone health

Introduction
Menopause is a normal part of the aging process. It is the natural cessation of menstruation that usually occurs between the ages of 45 and 55 and can increase a women's risk of developing osteoporosis, a condition in which bones became thin and may fracture easily. The drop in estrogen levels that occur around the time of menopause results in increased bone loss. It is estimated that women loses 3 to 5 percent of her bone mass every year during the first 5 year after menopause. After 5 years, she loses from one to two per cent of bone mass yearly. Smoking, heavy drinking, and not getting enough calcium in the diet can increase a woman's risk of bone loss [1].

Menopause signifies the end of woman's reproduction life and ovaries stop releasing eggs. A woman is considered menopausal once she has gone a year without having a menstrual period. Follicle stimulating hormone (FSH) and pituitary gland as part of the normal menstrual cycle stimulate the ovary to produce estrogen and progesterone and to release an egg. As a woman ages, her ovaries not respond to FSH or LH as strongly as they used over time, less and less estrogen and progesterone are produced and the woman stops releasing eggs.

Peak bone mass is reached around the age of 25 to 30 years, when the skeleton has stopped growing and bones are at their strongest and thickest stage. The female sex hormone, estrogen plays an important role in maintaining bone strength. Estrogen levels drop during menopause, at around the age of 50 years resulting in increased bone loss. If a woman's peak bone mass before menopause is less than ideal, any bone loss that occurs during menopause may result in osteoporosis. Research suggests that about half of all women over the age of 60 years will experience at least one fracture due to osteoporosis [2].

Reduction in estrogen at menopause causes increased osteoclastic bone resorption as osteoclasts predominate over osteoblasts. Bone loss may continue for 5-10 years after menopause. There can be a difference in bone mass of up to 5 percent between men and women over the age of 60. Postmenopausal osteoporosis, the most common type of bone loss was first described in 1941 by Albright and Coworkers. It is caused primarily by a sharp decrease in estrogen levels that leads to an increased rate of bone remodeling (both resorption and formation. The risk of developing osteoporosis after menopause is determined largely by the peak bone mass reached at young adult age and by the rate of bone loss after menopause [3].

India has a large population, which has already crossed the 1 billion mark with 71 million people over 60 years of age and the number of menopausal women about 43 million. Projected figures in 2026 have estimated the population in India will be 1.4 billion, people over 60 years 173 million, and the menopausal population 103 million [4].

Health issues in India are always on a large scale and menopause is no exception. As one of the worlds's most populated countries, India faces a variety of challenge with menopause such as osteoporosis, hypertension, diabetes, cardiovascular diseases etc. Thus, the menopause is being the most important physiological ageing risk factor, the present study in focused on eliciting the menopausal related issues and the effect on bone mineral density and bone health.

Materials and Methods

The present research focused on evaluating the effect of menopause on estradiol levels and bone mineral density among women. For this, the comparative study was conducted among pre and postmenopausal women to find out the changes in the female estrogenic hormone and bone health. The sample was randomly selected from Tirupati urban town, South India aged 35 to 74 years who grouped into four age groups viz., 35 to 44 (n=60), 45 to 54 (n=80), 55 to 64 (n=80) and 65 to 74 years (n=40) with the total sample size of 260 members.

Interview method was followed to identify menopausal condition and the age at menopause. The method of serum estradiol was assessed through RIA method. The bone health was evaluated through testing Bone Mineral Density (BMD) using Quantitative Ultra Sound (QUS) bone densitometry measured at calcaneous bone for the women who voluntarily participated in the study during free BMD campaigns at local orthopedic hospitals.

Results and discussion

The section deals with the menopausal condition, age at menopause, estradiol levels in pre and postmenopausal women in relation to bone health. The data obtained was interpreted and presented in tables. The findings were illustrated separately under different sub-heads.

Distribution of pre and post-menopausal women

The age at menopause (AMP), being an important parameter is discussed in terms of menopause nature including premature, early, ideal and late menopause against pre-menopausal women who are still menstruating without onset of menopause. Based upon the onset of menopause, the menopausal women can be classified into premature, if the menopause attained before 40 years, early menopause between 40 to 44 years, ideal between 45 and 50 years and late menopausal of more than 50 years [5]. The number and distribution of women based menopausal status are presented in the table no 1.

Table 1: Menopausal status: Percent distribution of pre and postmenopausal women by age at menopause (AMP) nature of select women groups

Age Group (Years)	Pre-Meno pause N (%)	Age at menopause (AMP)nature (Years)								Total Age Wise Mean AMP& ± SD
		Premature (< 40)		Early(40-44)		Ideal (45-50)		Late(> 50)		
		n (%)	Mean AMP &± SD	n (%)	Mean AMP &± SD	n (%)	Mean AMP &± SD	n (%)	Mean AMP &± SD	
35-44(n=60)	60(100)	0(0)	Nil	0(0)	Nil	0(0)	Nil	0(0)	Nil	Nil
45-54(n = 80)	7(9)	8(10)	33.13± (5.14)	19(24)	42.05± (1.08)	32(40)	46.53± (1.34)	14(17)	51.21± (1.97)	46.29± (5.55)
55-64(n = 80)	0(0)	7(9)	38.00± (1.16)	23(29)	42.39± (1.08)	33(41)	47.15± (1.20)	17(21)	51.77± (1.17)	45.98± (4.32)
65-74(n = 40)	0(0)	5(13)	36.40± (0.89)	13(32)	42.46± (1.20)	13(32)	46.77± (1.17)	9(23)	51.44± (1.13)	45.13± (4.84)

The important observation noted that all the urban younger women are pre-menopausal without facing the menopausal state. Whereas, only a small portion of middle aged women around 9 percent in the age group of 45 to 54 years were premenopausal. All the aged and elderly women of more than 55 years experienced the onset of menopause. The data was clear that the onset of menopause usually began from the middle age of 45 years or later of age.

Around one tenth or more of women found to be premature menopausal women due to the onset of menopause even before the age of 40 years with a range of 9 to 13 percent. The other important finding highlighted that about one fourth to one third of them were early menopausal women. Majority of women had reached their menopause between 45 to 55 years. However, considerable number around 17 to 23 percent of them had late menopause after the age of 50 years.

Etradiol levels

The major effect of estrogen on bone remodeling in adult humans may be due to decrease in bone resorption rather than to modulate bone formation. Despite presence of estrogen receptor in osteoclasts, it is possible that the binding of estrogen to receptors in osteoblasts regulates osteoclast function indirectly, which would add a second layer of regulation to the direct regulation of osteoclasts by estrogen and provide an opportunity for cell to cell interactions.

Based on the role of estrogen in bone metabolism, mainly estradiol as potent form of estradiol was purposively analysed in select groups of women. The female hormone secreted in the form of estradiol was analyzed in the serum. The data was interpreted in terms of premenopausal and menopausal women who were categorized as premature, early, ideal and late and expressed age wise from younger to elderly and presented in table no-2.

Table 2: Mean Estradiol levels- Percent distribution of pre and postmenopausal women by age at menopause (AMP) nature of select women groups

Age Group (Years)	Mean Estradiol levels (pmol/l)					
	Pre-menopause Mean ± SD	Premature(< 40) Mean ± SD	Early(40-44) Mean ± SD	Ideal(45-50) Mean ± SD	Late(> 50) Mean ± SD	Total Age wise Mean± SD
35-44(n=60)	104.22±5.35	Nil	Nil	Nil	Nil	104.22±5.35
45-54(n = 80)	98.67±2.56	68.96±9.38	51.35±5.49	51.73±6.33	52.17±6.18	56.34±14.03
55-64(n = 80)	Nil	56.77±8.19	55.80±5.57	47.33±7.73	41.80±4.28	49.42±8.52
65-74(n = 40)	Nil	42.34±3.70	40.83±3.16	45.84±3.84	47.95±2.33	43.37±3.81

The striking point to be observed that there was a drastic decline in estradiol levels among postmenopausal women which was about half of the level. This was clearly evidenced by the mean estradiol value of 104.22 pmol/l followed by

sharp reduction in middle aged women calculated as 56.34 pmol/l. The estradiol values found to be still lowered in aged and elderly women. The estrogen deficiency status was much higher in premature menopausal women and early postmenopausal women.

The findings well demonstrated that the decline in estrdiol was obvious which could not be arrested. That was the reason it was essential to find alternative strategy to minimize the rate of reduction. Incorporation of calcium and phytoestrogenic rich foods, adequate exercise and adopting healthy life style would be helpful to attenuate bone loss and promotion of bone retention to lead the life with sturdy bones.

Bone health status

The major pathogenic factor of osteoporosis, the 'estrogen deficiency' is first detected by Albright *et al* (1941). Estrogen deficiency during menopause causes rapid bone loss, especially in the early years after menopause. It is well known that estrogen deficiency induces the synthesis of cytokines by the osteoblasts, monocytes and T-cells and thereby stimulates the bone resorption by increasing the osteoclast number and osteoclast activity. The increased bone resorption consequent to estrogen deficiency causes osteoporosis in post-menopausal women. In case of premenopausal women, the sufficient estradiol levels inhibit the synthesis of cytokines and thereby lower the bone resorption rate [6].The concept that estrogen deficiency is critical to the pathogenesis of osteoporosis was based initially on the fact that postmenopausal women, whose estrogen levels naturally decline, are at the highest risk for developing the disease.

Osteoclast apoptosis is regulated by estrogens. With estrogen deficiency, the osteoclasts live longer and are therefore able to resorb more bone. In response to the increased bone resorption, there is increased bone formation and a high-turnover state develops which leads to bone loss and perforation of the trabecular plates. Estrogen has multiple other effects that relate to the skeleton. For example, enhanced intestinal calcium absorption can be beneficial to bones. Estrogen protects the bone from the resorptive effects of parathyroid harmone (PTH). Estrogens may interact with mechanical forces to build bone [7]. In view of importance of estradiol in bone metabolism, the present study aimed at finding out the association of estradiol and menopausal for which estradiol levels were evaluated among premenopausal and postmenopausal women in terms of premature, early, ideal and late menopause conditions. The results obtained were pooled and presented in table no-3.

Table 3: Bone health status of women based on menopausal condition and nature of menopause

Age Group (Years)	Mean BMD levels					
	Pre-menopause Mean ± SD	**Premature(< 40) Mean ± SD**	**Early(40-44) Mean ± SD**	**Ideal(45-50) Mean ± SD**	**Late(> 50) Mean ± SD**	**Total Age wise Mean± SD**
35-44(n=60)	-0.75±0.62	Nil	Nil	Nil	Nil	-0.75±0.62
45-54(n = 80)	-0.60±0.13	-2.07±1.01	-1.69±0.76	-0.54±0.40	-0.38±0.12	-0.94±0.83
55-64(n = 80)	Nil	-2.63±0.44	-1.71±0.88	-0.80±0.63	-0.66±0.52	-1.19±0.91
65-74(n = 40)	Nil	-3.04±0.67	-2.73±0.72	-1.93±0.61	-2.04±0.91	-2.65±0.82

The results from the table illustrated that bone health was being deteriorated with the ageing process as evidenced by lowered bone mineral density from young to elderly irrespective of menopausal condition. Premature menopausal women were more prone to maximum bone loss followed by early menopausal women due to arrival estrogen deficiency status at much earlier period due to onset of menopause earlier before the age of 45 years. Menopause is the natural physiological change associated with ageing process among women. This condition leads to reduction in the major female hormone, estradiol which plays a crucial role in bone formation. With the slowing down of bone formation, bone health becomes gradually deteriorated with the lowering of bone mineral density.

On the other hand the conditions of ideal and late menopausal women were exposed to relatively higher period of estrogen exposure. Being spent more number of estrogenic beneficial years, both conditions of menopausal women had better bone health status due to retention of comparatively better bone mineral density. The lowered levels of serum estradiol accelerated the osteoclastic activity and enhanced the rate of bone loss resulting in lowered bone densities which lead to conditions of more of bone loss and deterioration. This underlying mechanism is responsible for the decline in the bone densities with progressive age indicating a direct association of serum estradiol and bone mineral density in women.

The findings denoted an inevitable decrease in the levels of serum estadiol concentrations after the age of 45 years in postmenopausal women as it was an unavoidable physiological process found in women with the cessation of menstrual cycle. This condition was accompanied by drastic reduction of ovarian hormones especially serum estradiol levels. The cited results clearly represented a positive association of serum estradiol with that of bone mineral density and minimize the bone resorption levels through reducing osteoclastic activity. The measures to improve estrogenic activity such as hormone replacement therapy, phytoestrogenic supplementation coupling with physical activity may be helpful to the postmenopausal women in enhancing the levels of estrogens mainly estradiol in the serum and to increase the rate of bone mineral density which will reduce the further risk of bone deterioration and the onset of osteoporosis at an earlier age.

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