

## ORIGINAL ARTICLE

## BONE STRENGTH AND ITS DETERMINANTS IN PERI- AND POSTMENOPAUSAL WOMEN

Farida Hafeez, Madiha Ahmad, Shahid Hasan, Rukhshan Kurshid\*

Department of Physiology, CMH Lahore Medical College, \*Department of Biochemistry, Fatima Jinnah Medical College, Lahore, Pakistan

**Background:** Diminished bone strength increases the frequency of osteoporosis and fragility fractures. Weight and gonadal status are important determinants of bone mass in women. This study tried to find out the bone strength and its determinants in peri- and postmenopausal age groups of women. **Methods:** One hundred and twenty females with age range 25–66 years were included in the study. According to their age and menstrual status they were divided into premenopausal (30) perimenopausal (50) and postmenopausal (40). Body Mass Index (BMI) and bone related blood parameter, serum calcium, magnesium, inorganic phosphorus, alkaline phosphatase and estradiol were estimated. Bone mineral density was taken by peripheral densitometer. **Results:** Blood chemical parameters were not significantly different in these groups. The *p*-value of serum estradiol was highly significant in peri- and postmenopausal groups. BMI was significantly high in postmenopausal as compared to pre and perimenopausal groups. **Conclusion:** Early menopause, low levels of oestrogen and BMI values can all affect the health of bones in elderly women.

**Keywords:** Osteoporosis, perimenopausal, postmenopausal, bone mineral density, body mass index, oestrogen

## INTRODUCTION

Bone health, characterised by its mass, density, and micro-architectural qualities, is maintained by a balanced system of remodelling.<sup>1</sup> The continual deposition and absorption strengthen and rearrange the shape of the bone for mechanical support. Bone stress also determines the shape of the bones under certain circumstances. Any combination of change in the rates of bone formation or absorption could cause an increase or decrease in bone mass.<sup>2</sup>

Adult women have less bone mass than adult men, and after menopause they lose it more rapidly than men of comparable age do. Consequently, they are more prone to development of serious osteoporosis.<sup>3</sup> Although it affects the whole skeleton, the spongy bones of vertebrae and wrist are more vulnerable. The femur particularly its neck is very susceptible to fracture.<sup>4</sup> Fractures in elderly individuals are associated with a mortality rate of 12–20% and half of those who survive require prolonged expensive care. The incidence of osteoporotic fractures is constantly increasing due to the increase in life expectancy.<sup>5</sup> Osteoporotic fractures usually occur 10 to 20 years earlier in Indian/Pakistani men and women compared with their western Caucasian counterparts.

Many factors more or less dependent on each other are known to influence bone mass. These determinants classically include race, age, gender, nutrients, endocrine factors and mechanical forces like physical activity and body weight.<sup>1</sup> All these factors are associated with bone health.

Menstrual status is an important determinant of bone mass. It was reported by Khan and Syed that postmenopausal women had significantly lower bone

mass than that of pre- and perimenopausal women. So identification of postmenopausal women at high risk of fracture therefore is a priority and is especially for those who can benefit from early intervention to maintain or to increase bone mass and thus reduce the risk of fractures.<sup>6</sup>

## MATERIAL AND METHODS

One Hundred and twenty females with age range 25–66 years were included in the study. The proforma was filled by those women including their age, parity and menstrual status. BMI (body mass index) was calculated for them by taking their heights weights. Five millilitres of blood was taken from each subject. Bone mineral density was taken by heel densitometer (Hologic Sahara). BMD of right heel was measured for all the subjects. The values were taken in T-score. According to machine T-score +1 to -1 was considered Normal, -1 to -2.4 as Osteopenia and below -2.4 as Osteoporosis.

Blood parameters, serum calcium, magnesium, inorganic phosphorus, alkaline phosphate were estimated by auto-analyser and estradiol by ELIZA. The data was compared by student's *t*-test using SPSS-10.

## RESULTS

According to their age and menstrual status those women were divided into three groups, Pre-menopausal (30), perimenopausal (50) and postmenopausal (40). Demographic characteristics of pre-, peri- and postmenopausal women are tabulated (Table-1). The mean age of pre-, peri- and post-menopausal women was 30, 45 and 58 years respectively. Their age at menarche was 13 years. The mean age of menopause in the postmenopausal group (according to their menopausal

history) came out to be 47 years. BMI of pre and perimenopausal women was less than 30 and of postmenopausal women was greater than 30. It is significantly higher than the pre menopausal group.

Variation in bone related parameters, i.e., serum calcium, magnesium, inorganic phosphorus, estradiol and T-score in peri- and postmenopausal women are tabulated. Their levels are compared with the levels of pre- and perimenopausal women (Table-2). The level of calcium and phosphorous were non-

significantly higher in peri- and postmenopausal women as compared to premenopausal women (controls). Level of magnesium was not changed. On the other hand level of alkaline phosphatase and estradiol were less in both peri- and post- menopausal women as compared to premenopausal women (controls) but the significant difference was only observed in case of serum estradiol. BMD T-score of peri- and post-menopausal women were also non-significantly decreased in peri- and postmenopausal women compared to their controls.

**Table-1: Demographic characteristics of peri- and postmenopausal women (Mean±SD)**

Variables	Premenopausal women (30)	Perimenopausal women (50)	Postmenopausal women (40)
Age at Menarche (years)	13.02±1.27	13.02±1.27	12.97±1.24
Present age (years)	30.96±4.15	45.15±3.58	58.18±5.85
Age at Menopause	-	-	47.03±7.10
BMI	27.90±5.84	27.20±4.08	32.12±3.87*

\* $p < 0.05$

**Table-2: Variation in bone related parameters in peri- and postmenopausal women (Mean±SD)**

Blood Parameters	Premenopausal women (n=30)	Perimenopausal women (n=50)	Postmenopausal women (n=40)
Calcium (mg/dL)	8.26±0.56	8.30±0.52	8.40±0.63
Magnesium (mg/dL)	2.30±0.20	2.35±0.23	2.28±0.25
Inorganic Phosphorus (mg/dL)	3.86±0.59	4.32±0.54	4.19±0.67
Alkaline Phosphate U/L	217.20±58.87	214.23±65.64	211.03±51.82
Estradiol (pg/ml)	84.83±75.04	46.59±40.86*	47.27±62.23*
BMD (T-score)		-0.82±0.77	-1.22±1.13

\* $p < 0.001$  highly significant between pre- and peri-, pre-, and postmenopausal groups

## DISCUSSION

Present study observed that the mean age of perimenopausal women was 45 years, and their age range was 40 to 50 years. The age of perimenopausal women of our study is in accordance with the study of Bainbridge, who included 50 years old women for the assessment of risk factors of osteoporosis among perimenopausal groups.<sup>7</sup> The present study is also in accordance with a study, which included Spanish women having an age range of 40 to 77 years for both peri- and post-menopausal group.<sup>8</sup> It has been reported that cross-sectional or longitudinal studies of women aged 40 years and older used the definition of perimenopause as 3–11 month amenorrhea or irregular periods, but the prior probability of perimenopause is directly related to woman's age.<sup>9</sup> We therefore considered 40 years of age as perimenopausal age.

In our data the mean age of postmenopausal women was 58 years. According to their history of menopause the mean age of menopause came out to be 47 years. It is in accordance to the study in Saudi Arabia,<sup>10</sup> which found the mean age of menopause 48 years and stated that early or late onset of menopause is related to osteoporosis. This age of menopause among Saudi women is lower than that in western countries. In addition to cultural differences, genetics play a role in determining the age of menopause and development of osteoporosis. The present study is in contrast with

the western study, reporting the menopausal age greater than 58.<sup>11</sup> It is reported by a group of workers that early menopause may be a risk factor for osteoporosis. It was also found that an increased risk for low BMD (osteopenia and osteoporosis) was associated with age and menopausal status.<sup>12</sup>

Many physiological risk factors are associated with the fractures including personal and family history of fractures, low body weight, low physical activity and low intake of calcium.<sup>13</sup> The present study also takes in consideration the physiological risk factors like body weight, BMI. It was observed that the mean body weight of postmenopausal women was more than that of premenopausal, which lead to the increase BMI in this group. This may increase the risk of ankle fractures. It has been reported that increased body weight generates greater force during a fall, twist or turn, resulting in a greater probability of fracture.<sup>14</sup>

Physical activity is a way to prevent osteoporosis because it can regulate bone maintenance and stimulate bone formation including the accumulation of mineral thus reducing the overall risk of fractures. Physical activities continue to stimulate increase in bone diameter through out the life span. The increase in bone diameter diminishes the risk of fractures by counter acting the thinning of bones and increase in bone porosity.<sup>15</sup>

Lack of physical activity is an important factor for increasing BMI. The study by Delaney *et al*

suggested that menopausal women can benefit from non-pharmacological interventions to reduce the risk of fractures, including a balanced diet and regular exercise.<sup>11</sup>

We observed that the level of alkaline phosphatase was subsequently less in peri- and postmenopausal women. Haliloglu B *et al*<sup>13</sup> reported that one of the underlying mechanisms of osteoporosis may be a mechanistic link which cannot be detected by BMD or biochemical markers like alkaline phosphatase.

Level of serum estradiol was decreased significantly in both peri- and postmenopausal women as compared to the level of estradiol of premenopausal women (control). It was observed that the level of serum estradiol was almost same in both peri- and postmenopausal women. A study reported that in menopause the limitation of the capacity of skeleton to adapt to mechanical stress of exercise is due to altered hormonal status.<sup>14</sup> One study found that oestrogen essentially prevents this bone loss, and it continues to be prevented for as long as estrogens are taken.<sup>16</sup> Another study proposed that bone osteoblasts are more sensitive to age-related oestrogen loss than are the osteoclasts, so the homeostasis of this bone remodelling eventually shifts. They found that oestrogen deficiency promotes bone loss at any age, it increases the life span of osteoclasts and decreases the life span of osteoblasts and this may lead to negative balance and decrease bone formation.<sup>17</sup>

Value of T-score was non-significantly less in both peri- and postmenopausal women as compared to premenopausal women. A study reported that decrease in bone mineral density associated with menopause progresses for at least ten years, and early menopause and aging increase the risk of osteoporosis.<sup>18</sup>

Although low peak bone mass is a risk factor for postmenopausal osteoporosis and fractures, the relationship between low BMD and fracture risk during the premenopausal time period is not fully understood.<sup>1</sup> Many studies tried to find out the relationship with menstrual status. A study instituted that low BMD is associated with an increased relative risk of fracture in postmenopausal women.<sup>18</sup> Another study<sup>19</sup> reported that although central BMD testing can account for approximately 60–70% of the variation in bone strength, it could not capture other aspects of bone quality such as bone micro-architecture, which may be preserved in younger women, thus protecting them from fracture as compared to women with peri- or postmenopausal status.

## CONCLUSION

The demographic characteristics like low physical

activity, and increased BMI may be a risk factor in developing osteopenia. The bone related parameters, especially decreased level of alkaline phosphatase, decreased value of T-score and decreased level of hormone estradiol may be associated with fragility fractures. Further research is needed on a large group of women and including other bone related hormones like leptin, adiponectin etc. to reach a better conclusion.

## REFERENCES

1. Usmani S, Shaid Z. An over-view of postmenopausal osteoporosis. *Pak J Med Sci* 2004;20(3):270–5.
2. Guyton C, Hall E. Bone and Teeth. In: *Text book of Medical Physiology*, India: Elsevier Inc.; 2006. p981–2.
3. Ganong WF. Hormonal control of calcium metabolism and physiology of bone. In: *Review of Medical Physiology*, Singapore: The McGraw-Hill; 2005. p386–7.
4. Elaine N. Bones and Skeletal Tissues. In: *Human Anatomy and Physiology*. India: Pearson Education Inc.; 2006. p193–4.
5. Gambacciani M, de Aloysio D, Elia D. Quantitative ultrasound of bone in the management of postmenopausal women. *Maturitas* 2004;20(47(2)):139–49.
6. Khan A, Syed Z. Bone densitometry in premenopausal women. *J Clin Densitom* 2004;7(1):85–92.
7. Bainbridge KE, Sower M, Lin X, Harlow SD. Risk factors of low bone mineral density and the 6-year rate of bone loss among premenopausal and perimenopausal women. *Osteoporos Int* 2004;15(6):439–46.
8. Ubeda N, Basagoiti M, Alonso-Aperte E, Varela-Moreiras G. Dietary food habits, nutritional status and lifestyle in menopausal women in Spain. *Nutr Hosp* 2007;22(3):313–21.
9. Bastain LA, Smith CM, Nanda K. Is this woman perimenopausal? *JAMA* 2003;289(7):895–902.
10. Addar M, Desouki M, Babay Z. Correlates of age at menopause and osteoporosis in Saudi women. *Clin Exp Obstet Gynecol* 2005;31(2):135–7.
11. Delaney M. Strategies for the prevention and treatment of osteoporosis during early postmenopause. *Am J Obstet Gynecol* 2006;194(2 Suppl):S12–23.
12. Smeets-Goevaers CG, Lesusink GL, Papapoulos SE, Maartens LW, Keyzer JJ, Weerdenburg JP, *et al*. The prevalence of low bone mineral density in Dutch perimenopausal women. *Osteoporos Int* 1998;8(5):404–9.
13. Haliloglu B, Aksungur FB, Ilter E, Peker H, Akin FT, Ozekici U. Relationship between bone mineral density, bone turnover markers and homocysteine, folate and vitamin B12 levels in postmenopausal women. *Arch Gynecol Obstet* 2010;28(4):663–8.
14. Voltola A, Honkanen R, Kroger H. Life style and other factors predict ankle fracture in perimenopausal women. *Bone* 2002;30(1):238–42.
15. Borer KT. Physical activity in the prevention and amelioration of osteoporosis in women: interaction of mechanical, hormonal and dietary factors. *Sports Med* 2005;35(9):779–830.
16. Masi L, Bilezikian JP. Osteoporosis: new hope for the future. *Int J Fertil Womens Med* 1997;42(4):245–54.
17. Ostrowska Z. Menopause, obesity, and bone status. *Postepy Hig Med Dosw (Online)* 2009;63:39–46.
18. Gourlay M, Brown S. Clinical consideration premenopausal osteoporosis. *Arch Intern Med* 2004;164(6):603–14.
19. Kanis JA. Diagnosis of osteoporosis and assessment of fracture risk. *Lancet* 2002;359:1929–36.

## Address for Correspondence:

Dr. Farida Hafeez, Department of Physiology, CMH Lahore Medical College, Lahore, Pakistan. Cell: +92-300-8536656

Email: farida.asif.malik@hotmail.com