BONE MASS MEASUREMENT AND FACTORS ASSOCIATED WITH RISK OF FRACTURE IN A GROUP OF PERI- AND POSTMENOUPAUSAL WOMEN

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Background: This study tried to find out the physiological risk factors as well as biochemical factors in a group of Pakistani peri- and postmenopausal women. **Materials and Method:** One hundred female subjects with age range of 40–52 years were included in the study. Female subjects were divided into two groups, i.e., 65 women with perimenopausal status age range 40–52 years old and 35 women with post menopausal status age range of 50–60 years. Detailed histories of subjects including factors that may contribute in bone fracture were recorded. Bone density was scanned. Blood parameters like serum calcium, alkaline phosphatase, total protein and uric acid were estimated. **Results:** It was found that 70% of perimenopausal women belonging to class B were physically active. Hormonal replacement therapy (HRT) was observed in 25–30% of both groups. On the other, only 15% of both groups used oral contraceptives. Family history was found to be only in 10% of both groups. Level of serum calcium of perimenopausal/postmenopausal was less than normal control subject. Although the level of alkaline phosphatase was increased in perimenopausal women as compared to postmenopausal women and normal control subjects. Bone density of both peri- and postmenopausal women significantly decreased as compared to T score of normal control. **Conclusion:** It was concluded that a number of factors are predictive of future risk for the development of osteoporosis in women of reproductive age. Given the severity of the medical consequences of osteoporosis, the medical community needs to assess all women for these risk factors during their perimenopausal years.

Key Words: Bone density, peri- and postmenopausal status, risk factors.

INTRODUCTION

Osteoporosis is a major public health problem affecting one in three women over the age of fifty. Decreased bone density associated with osteoporosis makes bones brittle, and spinal fractures affect one in every three women, wrist and hip fractures one in every six. This leads to rapid deterioration in health and often death. The Older Women's League reports that 90% of hip fractures are due to osteoporosis. Half of the women who suffer hip fractures lose the ability to walk independently and up to one third become totally dependent.[1]

The consequences of osteoporosis are more evident in postmenopausal populations; loss of bone density begins in the perimenopausal years.[2] Bone mineral density, a key determinant in osteoporotic fracture in adult women, is a reflection of the peak bone mass attained in young adulthood and the bone mass lost during the perimenopausal and postmenopausal years.[3] When calcium balance is maintained, little or no loss of BMD occurs. However, because osteoblasts are more sensitive to age-related oestrogen loss than are osteoclasts, the homeostasis of this remodelling cycle eventually shifts.[4]

Osteoporosis may result: Bone matrix continues to be formed, but in amounts that are insufficient to fill the cavities left by resorption. The trabeculae, which are anchoring strands of connective bone tissue, become thin and fragile and may fracture. It has been suggested that the biomechanical competence of the trabecular matrix is dependent not only on the absolute amount of bone present but also on the strength of its own microarchitecture.[5,6]

Most longitudinal and cross-sectional studies have suggested that the pathogenesis of low BMD begins prior to menopause. Oestrogen deficiency has also been associated with low BMD.[7] Oestrogen deficiency in premenopausal women may induce excessive resorption and result in reduced peak bone mass. Such a lack of this hormone may be associated with a variety of conditions, including excessive exercise, anorexia nervosa, and hyperprolactinemia.[8,9]

Bone related disorders are white or Asian women (Genetic factors)**,** low BMD, maternal history of hip fracture, early menopause, prolonged amenorrhoea, pre-existing fracture, low trauma fracture since age 45, medical conditions predisposing to osteoporosis, high bone turnover and sedentary life style.[10,11] Conversely, blood level of calcium, alkaline phosphatase, uric acid, proteins and bone density may play a role in development/ prevention of osteoporosis.[12,13]

Present study tried to find out the physiological risk factors as well as biochemical factors in a group of Pakistani peri- and postmenopausal women.

MATERIALS AND METHOD

One hundred female subjects with age range of 40–52 years included in the study. The subjects were the teaching faculty members of Fatima Jinnah Medical College, Lahore, Orthopaedic Ward of Sir Ganga Ram Hospital, Lahore and staff of a local clinic of Lahore. Female subjects were divided into two groups, i.e., a group of 65 perimenopausal status with age range 40–52 years old and the other group was of 35 post menopausal status with age range of 50–60 years. Twenty-five women with no known risk factors and normal levels of biochemical parameters were considered as controls or normal subjects.

Detailed histories of subjects including factors that may contribute in bone fracture were recorded. Bone density was scanned by bone scanner after applying gel on the right heel. Blood parameters like serum calcium, alkaline phosphatase, total protein and uric acid were estimated by standard kits of Merck. T score less than -2.0 indicates risk factor.

Statistical analysis:

Mean, standard deviation and standard value was calculated using computer program SPSS. Value of significance was calculated using student's *t*-test.

RESULTS

Risk factors of bone fractures are tabulated in Table-1. It was found that 70% of perimenopausal women were physically active while only 10% were women also carry out exercise. Conversely only 50% post-menopausal women were active (walking habit), 5% have an exercise along with exercise but remaining 45% have no interest in exercise or walk. It was observed that only 20% of both perimenopausal women belonged to class A, 70% belonged to class B and 10% belonged to class C. On the other hand, only 10% of both perimenopausal women belonged to class A, 80% belonged to class B and 10% belonged to class C. Hormonal replacement therapy was observed in 25–30% of both groups, whereas only 15% of both groups used oral contraceptives. Family history was found to be only in 10% of both groups. Parity was observed in 90% of both groups.

Table-2 shows that minimal age of perimenopausal women was 48 years and maximum age was 52 years. On the other hand, minimal age of postmenopausal women was 50 years and maximum age was 60 years. Level of serum calcium of perimenopausal/postmenopausal was less than normal control subject but this shows no significant difference. Although the level of alkaline phosphatase was increased in perimenopausal women as compared to postmenopausal women and normal control subjects but this shows no significant difference. Total serum protein was more or less same in both groups and in normal control subjects. Level of serum uric acid was nearly same in both groups of patients. However in comparison with the level of serum uric acid of normal control subject, it was non-significantly increased. Bone density was also noted by estimating the T-score. It was observed that T-score of perimenopausal women was significantly decreased ($p<0.001$) as compared to T score of normal control. On the other, T-score in postmenopausal women was also significantly decreased ($p<0.01$) as compared to T-score of normal subjects.

Table-1: Risk factors of bone fractures in Perimenopausal women

Parameters	Perimenopausal women (n=85)	Postmenopausal women (n=15)
Marital status	All married	All married
Age (yrs)	43.87±2.64	58.20±2.85
Height (ft)	5.27±0.31	5.10±0.22
Weight (Kg)	55.20±8.74	65.00±9.8
Body mass index	24.64±3.96	
Excess BMI	7.73±1.89	
Physical activity	70%	50%
Physical activity + Exercise	10%	5%
Sedentary life	20%	45%
Socio-economic status	Class A= 20% Class B= 70% Class C= 10%	Class A= 10% Class B= 80% Class C= 10%
Hormone replacement therapy (HRT)	51%	50%
HRT never taken	26%	25%
HET as Oral contraceptives	23%	25%
Family history	12%	10%
No family history	88%	90%
Parity	90%	89%
Infertile	10%	11%

Table-2: Bone density and blood biochemical parameters in perimenopausal/postmenopausal women

Parameters	Perimenopausal women (n=85)	Postmenopausal women (n=15)	Control (n=50)
Age (years)	44.07±4.01	55.75±1.71	46.8±13.5
Calcium (mg%)	7.34±0.35	7.50±1.73	8.24±0.12
Alkaline phosphatase (KAU)	11.29±18.29	7.25±3.50	7.15±2.46
Total protein (gm%)	7.33±0.47	7.55±0.30	7.18±0.11
Uric acid (mg%)	5.33±1.44	5.00±0.89	4.66±0.26
Bone density	-1.61±0.81**	-2.1±1.39*	0.95±0.45

*$p<0.001$=Significant difference, **$p<0.001$= Highly significant difference

DISCUSSION

Vertebral bone has been shown to achieve peak density between age 28 and 30 in healthy women; the proximal femur has been shown to gain most of its mass by late adolescence[14,15] hereafter, BMD begins its decline. The process accelerates during the 2 years prior to menopause, peaking during the first 3 years of menopause—when patients may lose 3% to 5% of their bone mass per year.[16] Such a trend helps to explain why an untreated 50-year-old woman has a 40% risk of osteoporotic fracture in her remaining lifetime (Epidemiology) with the risk of fracture rising exponentially with the decline in bone mass.[17] Present study shows that mean age of perimenopausal women was 44 years in post menopausal women was 55 years. However, another study demonstrated a hazard ratio of 1.9 for sustaining a subsequent fracture or fractures between age 35 and 57.[18] It is generally agreed that an osteoporotic fracture was significantly associated with the patient's age.[19]

Family history was also found in both perimenopausal and postmenopausal women. It is observed that 10% women have incidence of their first-degree relatives (mother and elder sister). Many studies are in accord with the number of studies. Data analyzed by a group of workers[20] suggest that genetic variations are influenced due to oestrogen-receptor locus, both singly and in relation to the vitamin D receptor gene. Another study found that familial resemblance for BMD, bone mineral content, and bone size were already present between daughters and their mothers before the daughters reached puberty.[21]

Physical study was more observed in perimenopausal women compared to post menopausal women. One study proved that physical activity as a way to prevent osteoporosis is based on evidence that it can regulate bone maintenance and stimulate bone formation including the accumulation of mineral, in addition to strengthening muscles, improving balance, and thus reducing the overall risk of falls and fractures.[22] Another study found that weight-bearing physical activity may reduce the risk of osteoporosis in women by augmenting bone mineral during the early adult years and reducing the loss of bone following menopause. A study[23] also observed repetitive activities, such as walking, may have a positive impact on bone mineral when performed at higher intensities. However, irrespective of changes in bone mineral, physical activities that improve muscular strength, endurance, and balance may reduce fracture risk by reducing the risk of falling.

Present study found low level of serum calcium in both group of patients, which may be due to low dietary calcium intake in childhood or in adolescence. A study concluded that milk consumption during childhood and adolescence have shown a statistically significant correlation between calcium intake and premenopausal BMD levels. One possible explanation on the role of calcium is that intake of this mineral may function as an 'enabler', allowing the skeleton to interact with both genetic and environmental characteristics.[24]

Level of serum uric acid was low in postmenopausal women as compared to perimenopausal women. A study reported that antioxidant defences are markedly decreased in osteoporotic women. The mechanisms underlying antioxidant depletion and its relevance to the pathogenesis of osteoporosis deserve further investigation.[25]

The data of present study shows a decreased level of alkaline phosphatase in postmenopausal women as compared to the level of alkaline phosphatase of perimenopausal women. A study observed that alkaline phosphatase and osteocalcin are phenotypic markers for early-stage differentiated osteoblasts and terminally differentiated osteoblasts, respectively.[26]

The T-score of perimenopausal women shows less bone mass density in perimenopausal women whereas the T-score of postmenopausal women shows a borderline of bone mass density. A study also found postmenopausal women with low bone mineral density at the hip or spine having a T score of less than -2.5, whereas T score of less than -2.0 have an additional risk factor.[27] Another study found that the prevalence of osteopenia and osteoporosis, according to T-score, was 54% and 14% respectively.[28] The reason given by a group of authors that oestrogen deficiency has also been associated with low BMD. Oestrogen deficiency due to oophorectomy without hormone replacement contributes to low postmenopausal bone mass and osteoporotic fracture.[24]

Total serum protein was found to be normal in both groups of patients. The study is in accord contrast to the study[29] who observed low protein level in both groups of patients. A study also found a normal level of protein but the study remarked that animal proteins are causally associated with an increased incidence of osteoporotic fractures.

CONCLUSION

A number of factors are predictive of future risk for the development of osteoporosis in women of reproductive age. Intervention into issues related to modifiable risk factors is important and bone density measurement may be indicated. Given the severity of the medical consequences of osteoporosis, the

medical community needs to assess all women for these risk factors during their premenopausal years.

REFERENCES

1. McCormick RK. Osteoporosis: integrating biomarkers and other diagnostic correlates into the management of bone fragility. Altern Med Rev. 2007 Jun;12(2):113–45.
2. Uetake T, Enomoto N. [Osteoporosis in elderly patients] Nippon Rinsho. 2007;65(5):933–8.
3. Sowers MFR, Boehnke M and Lancaster EK. Bone mass in relatives of osteoporotic patients. Ann Intern Med. 1988;109:870–3.
4. Mosley JR. Osteoporosis and bone function adaptation: Mechanobiological regulation of bone architecture in growing and adult bone, a review. J Rehabil Res Dev. 2000;37:189–99.
5. Eriksen EF, Langdahl BL. The pathogenesis of osteoporosis. Horm Res. 1997;48(suppl 5):78–82.
6. Akhter MP, Lappe JM, Davies KM, Recker RR. Transmenopausal changes in the trabecular bone structure. Bone. 2007;41(1):111–6. Epub 2007 April 10.
7. Wasnich D. Epidemiology of osteoporosis. In: Favus MJ, ed. Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism. 4th ed. Philadelphia Penn: Lippincott Williams & Wilkins: 1999: p 257–9.
8. Emaus A, Veierød MB, Furberg AS, Espetvedt S, Friedenreich C, Ellison PT, Jasienska G, Andersen LB, Thune I. Physical Activity, Heart Rate, Metabolic Profile, and Estradiol in Premenopausal Women. Med Sci Sports Exerc. 2008 May 2. [Epub ahead of print]
9. Sultana N, Sohail I and Yusuf F. Hormone replacement therapy in postmenopausal women. Rawal Med J. 2004;29(2):80–1.
10. Sowers MF, Galuska, DA. Epidemiology of bone mass in premenopausal women. Epidemiol Rev. 1993;15(2):374–98.
11. El-Hajj Fuleihan G. Osteoporosis: an overview of practice guidelines for bone density measurements and osteoporosis treatment strategies. Leb Med J. 1999;47:221–8.
12. Bonjour JP. Dietary protein: an essential nutrient for bone health. J Am Coll Nutr. 2005 Dec;24(6 Suppl):526S–536S.
13. Napoli N, Thompson J, Civitelli R, Armamento-Villareal RC. Effects of dietary calcium compared with calcium supplements on estrogen metabolism and bone mineral density. Am J Clin Nutr. 2007;85(5):1428–33.
14. Seeman E. Reduced bone density in women with fractures: contribution of low peak bone density and rapid bone loss. Osteoporosis Int. 1994;4(suppl 1):15–25.
15. Christiansen C. The different routes of administration and the effect of hormone replacement therapy on osteoporosis. J Fertil Steril. 1994;62(suppl 2):152S-156S.
16. Pouilles JM, Tremollieres F, Ribot C. [Vertebral bone loss in perimenopause]. In French. Presse Med. 1996;25:277–80.
17. Gallagher JC. Effect of early menopause on bone mineral density and fractures. Menopause. 2007;14(3 Pt 2):567–71.
18. Honkanan R, Tuppurainen M, Kroger H, Alhava E, Puntila E. Associations of early premenopausal fractures with subsequent fractures vary by sites and mechanisms of fractures. Calcif Tissue Int. 1997;60:327–31.
19. Rozenberg S, Frih L, Lang T, Koeger AC, Cabrol A, Gandjbackch I, *et al*. [Rheumatologic manifestations in heart transplant recipients. A cross-sectional study of 365 patients] Rev Rhum Ed Fr. 1993;60(1):10–5.
20. Willig M, Sowers M & Aron D. Bone mineral density and its change in white women: oestrogen and vitamin D receptor genotypes and their interaction. J Bone Miner Res. 1998;13:695–705.
21. Orwoll ES, Belknap JK, Klein RF. Gender specificity in the genetic determinants of peak bone mass. J Bone Miner Res 2001;16:1962–71.
22. 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.
23. Levis S, Altman R. Bone densitometry. Clinical Considerations. Arthritis Rheum 1998;41(4):577–87.
24. Sowers MF, Galuska, DA. Epidemiology of bone mass in premenopausal women. Epidemiol Rev. 1993;15(2):374–98.
25. Maggio D, Barabani M, Pierandrei M, Polidori MC, Catani M, Mecocci P, *et al*. Marked decrease in plasma antioxidants in aged osteoporotic women: results of a cross-sectional study. J Clin Endocrinol Metab. 2003;88(4):1523–7.
26. Kuo PL, Huang YT, Chang CH, Chang JK. Bone morphogenetic protein-2 and -4 (BMP-2 and -4) mediates fraxetin-induced maturation and differentiation in human osteoblast-like cell lines. Biol Pharm Bull. 2006;29(1):119–24.
27. Black DM, Cummings SR, Genant HK, Nevitt MC, Palermo L, Browner W. Axial and appendicular bone density predict fractures in older women. J Bone Miner Res. 1992;7:633–8.
28. Caudarella R, Vescini F, Buffa A, Sinicropi G, Rizzoli E, La Manna G, *et al*. Bone mass loss in calcium stone disease: focus on hypercalciuria and metabolic factors. J Nephrol. 2003;16(2):260–6.
29. Bonjour JP, Schurch MA, Rizzoli R. Nutritional aspects of hip fractures. Bone. 1996;18(3 Suppl):139S–144S.

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