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Correlation of age at menopause with bone mineral density in post-menopausal women: A prospective study

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Abstract
Background: Osteoporosis is a major public health problem as it is associated with substantial morbidity and socioeconomic burden.
Aims and Objective: To correlate the age at menopause with bone mineral density in post menopausal woman.
Materials and Methods: Two hundred postmenopausal women were studied at the Department of Obstetrics and Gynaecology, King Georges Medical University, Lucknow, between September 2015 to August 2016. A detailed questionnaire was filled which included details of demographic factors of the patient, detailed reproductive history including parity, number of living children, age at menarche, age at menopause, years since menopause, whether menopause was natural or surgical. BMD was measured in each woman at lumbar spine (L1-L4) by lunar Prodigy dual energy X Ray absorptiometry.
Results: A total of 72 (36%) women had osteopenia and remaining 123 (61.5%) had osteoporosis. Only 5 (2.5%) women had normal BMD status. Maximum (n=121) were in the 51-60 years age group. There was no significant relation between age and BMD. Proportion of women with osteoporosis was significantly higher in rural (70.3%) as compared to urban (41.9%) areas (p=0.001). Osteoporosis was seen in 82.6%women with > 4 parity (p=0.049). Mean age of menopause in women with normal BMD, osteopenia and osteoporosis was 44.60, 45.51and 43.85 years respectively. No significant association between period since menopause and BMD status could be seen. No significant association was observed either for total or for any of the BMD strata (p>0.05).With increasing duration since menopause a significant decline in T scores was observed (p=0.023) on overall assessment. However, this association was not significant statistically for different BMD strata (p>0.05).
Conclusion: The prevalence of osteoporosis was higher as compared to the world prevalence. The correlation between the age at menopause and BMD was significant in accordance with the various worldwide studies.

Keywords: Bone mineral density, osteoporosis, menopause

Introduction
Menopause is a normal part of life. It is a milestone just like puberty. According to Indian Menopausal Society, the average age of menopause in India is 47.5 years [1]. Menopause is associated with changes in the hypothalamic and pituitary hormones that regulate the menstrual cycle.
The principal health concerns of menopausal women include vasomotor symptoms, urogenital atrophy, osteoporosis, cardiovascular disease, cancer, cognitive decline and sexual problems. Amongst the various health concerns one problem which is often ignored but is of utmost importance is of bone loss. In postmenopausal women, the two major causes of bone loss are estrogen deficiency after menopause and age related decline in bone health [2].
The prevalence of low bone mass is more than 40% from the age of 40 years and increases to more than 62% by age 60 and 80% by the age of 65 years [3].
Osteoporosis a major public health problem and is associated with substantial morbidity and socioeconomic burden. According to World Health Organisation, osteoporosis is second only to cardiovascular disease as a global health care problem. It is a condition that can be prevented by increasing awareness about it and treated if diagnosed early and accurately.
Hence in present study we tried to correlate the age at menopause with bone mineral density in post-menopausal women.

Materials and Methods

Present cross sectional study was conducted on 200 postmenopausal women, up to 65 years of age over a period of one year at the Department of Obstetrics and Gynaecology, King Georges Medical University, Lucknow in collaboration with Department of Rheumatology, KGMU, Lucknow from September 2015 to August 2016

All post-menopausal women having natural menopause or surgical menopause following bilateral oophorectomy up to 65 years age who attended gynaecology O.P.D were enrolled after taking informed consent.

Women who did not give consent, women with either hysterectomy alone or hysterectomy with unilateral salpingooophorectomy, women more than 65 years of age as after this age bone loss is more dependant on age as compared to estrogen deficiency, study subjects with medical abnormalities affecting BMD like thyrotoxicosis, malabsorption, liver disease, kidney disease, diabetes mellitus, myeloproliferative disease, hyperparathyroidism, rheumatoid arthritis, women who were not ambulatory and women who were taking or have taken in past 1 year, drugs affecting bone mass like glucocorticoids, hormone replacement therapy, bisphosphonates, heparin, thyroxine, anticonvulsants, thiazides, cytotoxic drugs were excluded from the present study.

A detailed questionnaire was filled which included the demographic factors of the patient, detailed reproductive history including parity, number of living children, age at menarche, age at menopause, years since menopause, whether menopause was natural or surgical, personal history including history of exercise, smoking, alcohol intake, sun exposure daily. Any prior history of low trauma fracture or family history of low trauma fracture was noted.

All women were subjected to a routine gynecological examination. Subsequently all women underwent BMD examination at the Department of Rheumatology. BMD was measured in each woman at lumbar spine (L1-L4) by lunar Prodigy dual energy X ray absorptiometry.

The results were classified as normal, osteopenia and osteoporosis according to T score using NHANES database given by WHO. The reference range recommended by the IOF, International society of clinical densitometry, WHO and National Osteoporosis Foundation for calculating the T score in postmenopausal women is the NHANES III reference database in Caucasian women aged 20-29 years [4, 5].

All the data analysis was performed using IBM SPSS ver. 20 software. Quantitative data was expressed as mean ± standard deviation (SD) whereas categorical data was expressed as percentage. Cross tabulation and frequency distribution was used to prepare the table and Microsoft excel 2010 was used to prepare the required graph. Level of significance was assessed at 5% level.

Results

Out of 200 women, 72 (36%) had osteopenia and remaining 123 (61.5%) had osteoporosis, whereas only 5 had normal BMD.

Maximum (n=121) were in the 51-60 years age group, 48 were <50 years and 31 were >60 years. Among women up to 50 years of age, 62.5% were osteoporotic, 35.4% were osteopenic and 2.1% were having normal BMD. In women 51-60 years, 60.3% women were osteoporotic, 37.2% were osteopenic and 2.5% had normal BMD. In women >60 years of age 64.5% were having osteoporosis, 32.3% were osteopenic and 3.2% were with normal BMD. There was no significant relation between age and BMD.

Majority of women were from rural areas (69%). There were 62 (31%) urban women. Proportion of women with osteoporosis was significantly higher in rural (70.3%) as compared to urban (41.9%) areas (p=0.001).

Among women with ≤4 parity, 2.3% and 39% women were normal and osteopenic and 58.8% were osteoporotic. While in women with >4 parity 82.6% were osteoporotic. Statistically significant correlation was seen between parity and BMD status (p=0.049).

Mean age at menarche was 13, 12.79 and 12.63 years respectively among women with normal, osteopenia and osteoporosis. This association was not significant statistically.

Mean age of menopause in women with normal BMD, osteopenia and osteoporosis was 44.60, 45.51and 43.85 years respectively. Significant correlation was seen between age at menopause with BMD.

Table 1: Association between years since menopause and BMD Status

Years since menopause	Normal n=5		Osteopenia n=72		Osteoporosis n=123		Total n=200	
	No.	%	No.	%	No.	%	No.	%
<5 Years	1	5.0	11	55.0	8	40.0	20	10
5-10 Years	2	2.3	34	39.1	51	58.6	87	43.5
>10 Years	2	2.2	27	29.0	64	68.8	93	46.5

Table 2: Association of L1-L4 T-score with Age among women with different BMD status

S N	Age (Yrs)	Total			Normal			Osteopenia			Osteoporosis		
		N	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
1.	<50	48	-2.55	1.20	1	-1.00	.	17	-1.47	0.69	30	-3.21	0.93
2.	51-60	121	-2.44	1.23	3	0.03	0.58	45	-1.57	0.54	73	-3.07	1.10
3.	>60	31	-2.39	1.24	1	-0.20	.	10	-1.33	0.48	20	-3.04	1.01
P value		0.824			-			0.460			0.789		

Table 3: Association of L1-L4 T-score with Years since menopause among women with different BMD status

SN	Yrs since MP	Total			Normal			Osteopenia			Osteoporosis		
		N	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
1.	<5	20	-1.86	1.16	1	-1.00	.	11	-1.26	0.79	8	-2.79	1.04
2.	5-10	87	-2.39	1.13	2	0.20	0.71	34	-1.57	0.57	51	-3.03	0.92
3.	>10	93	-2.65	1.28	2	-0.25	0.07	27	-1.54	0.45	64	-3.20	1.13
P value		0.023			-			0.286			0.475		

Discussion

Denial of personal risk by postmenopausal women and restricted access to diagnosis and treatment before the first fracture occurs has been shown worldwide. Thus for the prevention and control of osteoporosis many epidemiological surveys have been conducted in various parts of India. Thus effective early identification of the BMD in postmenopausal women could improve the outcome by decreasing the risk of fracture.

It was found that out of 200 postmenopausal women who were enrolled in the study 123 (61.5%) had osteoporosis, 36% had osteopenia and 2.5% had normal BMD. According to International Osteoporosis Foundation, 30% of all the postmenopausal women had osteoporosis in United States and in Europe [6].

In India, there is no data on exact estimation of osteoporosis. Although various small studies have been conducted in various parts of India, prevalence of osteoporosis has been shown to vary from 8% to 62% in Indian women [7]. Amongst the studies conducted in North India, prevalence of osteoporosis was 62% in a study conducted in 2007 by Chhibber *et al.* [8]. A study by Marwaha *et al.* [9] in 2011 showed 42.5% of the females to be osteoporotic. The prevalence of osteoporosis from the present study was comparable to the Indian average but is higher than the world average.

Out of the 200 postmenopausal women in the present study, osteoporosis was seen in 62.5%, 60.3% and 64.5% of women upto 50 years, 51-60 years and >60 years of age groups respectively.

Other studies by Babu *et al.* [10] in 2009 and Unni *et al.* [11] in 2010 have shown that prevalence of osteoporosis increases with age, initially due to estrogen deficiency and later due to age related process. The association of age of the postmenopausal women with the overall BMD was not significant statistically (p=0.986) in the present study but significant association was seen between age and BMD at left forearm (p=0.038). On the contrary BMD at L1- L4, right and left neck femur did not show individual significant association with the age.

Demographic factors of the postmenopausal women were compared. There was statistically significant difference in prevalence of osteoporosis in relation to place of residence. In the present study 70.3% of rural women were osteoporotic as compared to 41.9% of the urban postmenopausal women. These results are similar to a study conducted in Indian population by Maletia *et al.* [12] in 2011. The study showed that the prevalence of disease was more common in rural population as compared to urban population. On the contrary, in a study by Das *et al.* [13] the BMD of urban and rural population reflected that 61.8% of the urban and 62.7% of the rural population were having osteopenia. Another study conducted in Eastern Poland [14] showed no statistically significant difference in mean values of BMD between urban and rural population.

In the present study, statistical significance was found in relation of BMD with the parity of woman. In women with ≤4 parity 58.8% were osteoporotic while in women with >4 parity 82.6% were osteoporotic (P=0.049).

In a systematic review on effect of parity on bone mineral density in postmenopausal women by Bayray *et al.* [14] in 2013, it was seen that out of the 19 studies evaluated, eight showed higher BMD in women with higher parity while six studies supported a negative effect of parity on BMD that is lower BMD in women with higher parity. Furthermore, five studies did not find any effect of parity on BMD.

A study on effect of early menopause on BMD by Francucci *et al.* [15] showed a significant association between age at menopause and years since menopause with BMD. It showed that women with early menopause had significantly lower BMD than normal and late menopause in 50-54 age groups. Beyond 55 years, early menopause, normal menopause and late menopause women had no differences in lumbar BMD values. Another study by Pouilles *et al.* [16] regarding influence of early age at menopause on vertebral bone mass showed that for the same chronological age, women with early menopause had a 15% lower BMD and a higher years since menopause than women whose menopause occurred later. Although a small effect of early menopause on bone mass cannot be entirely excluded, these data suggest that the amount of bone lost following menopause is the same irrespective of the age at which menopause occurs. Ito *et al.* [17] showed that in postmenopausal women, early menopause had a significant relationship to low BMD, and early menarche also had some relationship with high BMD. Another study by Zhonghua *et al.* [18] showed that later the menarche and earlier the menopause higher is the degree of osteoporosis.

In the present study, the mean BMD has shown a declining trend from being lowest at the left forearm followed by L1-L4, right neck femur and then left neck femur. This explains the observation that in postmenopusal women wrist fracture are first to occur followed by vertebral and lastly by neck femur [19].

Conclusion

In present study we tried to find the prevalence of osteoporosis and compare age at menopause with BMD. The prevalence of osteoporosis was higher as compared to the world prevalence and in range of Indian prevalence. The correlation between the age at menopause and BMD was significant in accordance with the various worldwide studies.

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