Obstetrics and Gynaecology Section An Observational Study to Evaluate the Changes in Bone Mineral Density of Women with Aging in a Tertiary Care Centre

MRIGANKA MOULI SAHA<sup>1</sup>, SUBIKAS BISWAS<sup>2</sup>, BANASREE BHADRA<sup>3</sup>

# ABSTRACT

**Introduction:** Osteoporosis has become a serious health threat for women. The osteoporosis related fracture rate as well as treatment cost is increasing in recent times due to aging population.

**Aim:** The aim of the present study was to investigate the risk factors of osteoporosis, identifying the risk group and the changes of Bone Mineral Density (BMD) in aging women.

**Materials and Methods:** This was a descriptive type crosssectional study conducted at the Institute of Postgraduate Medical Education and Research, Kolkata and College of Medicine, Kalyani, West Bengal from July 2013 to June 2016. Total 196 women who attended Gynaecology OPD were included in the study and interviewed regarding risk factors for developing osteoporosis. They were divided in two groups i.e., presence or absence of risk factors. Calculation of Body Mass Index (BMI) and T-score was done for all the subjects along with the Dual Energy X-Ray Absorpsiometry (DEXA) scan. It was a cross-sectional parallel group open level study. The tests were both sided with 95% confidence interval where p-value <0.05 was considered significant. Statistica and GraphPad InStat, version 3.0 were used for analysis.

**Results:** BMD T-score was less than -1.5 for all women and less than -2.5 after 40 years in the study group. However, in control population BMD T-score was less than -2.5 only after 50 years.

**Conclusion:** Osteopenia is a major concern for women in the presence of risk factors for osteoporosis even before menopause is achieved.

Keywords: Body mass index, Dual energy X-ray absorpsiometry, Menopause

## **INTRODUCTION**

Osteoporosis is a major health issue worldwide. Loss of bone mass and alteration of bone architecture are the two most typical features of osteoporosis. As the prevalence of osteoporosis is increasing, the osteoporosis related fragility is also rising and the related cost burden is expected to be doubled by 2050 [1]. More than 20% women over 50 years suffer from osteoporosis and nearly about 60% women suffer from osteopenia [2]. Vertebral and hip fractures are commonly encountered and these affect the health related quality of life [3]. It is speculated that the cost of treatment and the burden to the society will be nearly doubled by 2050 [4]. As per World Health Organization many risk factors have been identified under Fracture Risks Assessment Tool (FRAX) [5]. Some of them are modifiable and some are non modifiable. Currently the gold standard tool for assessing bone health is DEXA scan and calculation of z-score as well as T-score [6]. However, the osteoporotic fracture risk assessment is yet to be standardised. Particularly identifying the risk group population and preventive measures can reduce the osteoporosis related fracture incidence. Currently, the Physiatric Approach To Osteoporosis (PATO) project in Italy, Osteoporosis Risk Factor and Prevention-Fracture Prevention Study (OSTPRE-FPS) in Finland have been conducted in this regard [7,8]. Indian Council of Medical Research (ICMR) has already shown in a multicentric study that Indians have a lower mean bone mass than the North American counterparts [9]. The purpose of the study was to find out the prevalence of risk factors associated with osteoporosis in general population, identifying the risk group and calculation of BMD in the risk group as well as in general population.

### MATERIALS AND METHODS

This was a descriptive type cross-sectional study conducted at Institute of Postgraduate Medical Education and Research, Kolkata and College of Medicine, Kalyani, West Bengal. The study population consisted of the patients attending the Gynaecology Outpatient Department of the institution from July 2013 to June 2016. They were interviewed regarding the presence of risk factors of osteoporosis after obtaining an informed consent as per the prescribed proforma. These risk factors were modifiable and non modifiable. The modifiable risk factors were smoking, alcohol use (≥20 gm/day), sedentary life style (irregular physical activity and excessive amount of daily sitting, watching television, working on the computer, reading). The non modifiable risk factors included hyperthyroidism, Chronic Kidney Disease (CKD), use of systemic corticosteroid for prolonged time (more than 90 days), use of antiepileptic drugs, Chronic Liver Disease (CLD), inflammatory seropositive joint disorders, previous fractures, diabetes mellitus, use of aromatase inhibitors and antidepressants. BMI was calculated for all. Weight (in kg) was recorded on the platform and height (in meter) was measured with a wall marking. Calculation of BMI was done as follows:

#### BMI=weight (kg)/ height (m)<sup>2</sup>

The BMI less than 18.5 kg/m<sup>2</sup> were also considered as an independent risk factor for osteoporosis. The inclusion criteria were women aged between 18-80 years with any of the risk factors mentioned above, and not taking any antiresorptive medications like bisphosphonates or Selective Oestrogen Receptor Modulators (SERMs). Such 96 women were found in the study group. The exclusion criteria were women below 18 or above 80 years, any medical complication like hypertension, diabetes mellitus, premature menopause (before 40 years), taking any antiosteoporotic agents or calcium or vitamin D supplements or Hormone Replacement Therapy (HRT). Another 100 age matched women, not having any risk factor for osteoporosis were recruited as controls. All the patients were selected by simple random sampling technique. Measurement of BMD was done using DEXA scan and T-score was calculated. The BMD of the lumbar spine and hip joints was assessed in a single visit.

# **STATISTICAL ANALYSIS**

Data were presented as the total number of patients (n), mean value (mean), and Standard Deviation (SD), and percentage (%). SPSS (SPSS Inc., version x.0, Chicago, IL, USA) was used for the statistical analysis. The mean and SD values were computed over age (years), height (cm), waist circumference (cm), BMI (kg/m<sup>2</sup>), parity, diet were computed for each age group, separately and compared using t-tests and Wilcoxon-Mann-Whitney tests. The tests were both sided with 95% confidence interval where p-value <0.05 was considered significant. Numerical variables were compared between two groups.

# RESULTS

The mean age, height, waist circumference and mean parity were matched between study and control group without any significant statistical differences. The BMI was 21.4 (17.8-25.6) kg/m<sup>2</sup> in study group and 25.6 (20.8-27.5) in control group (p<0.05) which was significantly lower in the study group [Table/Fig-1]. Approximately, 60.4% patients were vegetarian in the study group compared with 32% patients (p<0.05) in control group which was significantly higher in the study group. Non vegetarians were 68% in the control group compared with 39.6% in the study group (p<0.05) which was significantly lower in the study group.

On analysis of the distribution of risk factors in the study group, 8.3% women were smokers, 43.7% women were leading sedentary lifestyle, and 4.2% women were taking regular alcohol of >20g/day [Table/Fig-2]. The BMI (kg/m<sup>2</sup>) was less than 18.5 in 6.2% patients in the study group. Moreover 14.6% patients were diabetic, 3.1% were suffering from liver disease, 2.1% patients were hyperthyroid, and 3.1% were suffering from CKD. Among the daily medications users 8.3% were taking systemic corticosteroid more than 90 days, 6.2% were taking antiepileptic agents, 33.3% were taking anti depressants.

The [Table/Fig-3] is showing the changes of BMD of lumbar spine according to different age groups. The entire study population were divided into total six groups i.e., 20-29, 30-39, 40-49, 50-59, 60-69, 70-77 years. The BMD of lumbar spine showing osteopenia in 20-29, 30-39, and osteoporosis in 40-49, 50-59, 60-69, 70-77 years age groups. Whereas in control group, we have found osteopenia in 30-39, 40-49 years of age and osteoporosis in 50-59, 60-69, 70-77 years age groups in lumber spine. [Table/Fig-4] showing the changes of BMD of hip joints according to different age showing osteopenia in 20-29, 30-39 years of age, and osteoporosis in 40-49, 50-59, 60-69, 70-77 years of age groups. In control group, we have found osteopenia in 40-49 age and osteoporosis in 50-59, 60-69, 70-77 years of age groups in hip joints.

### DISCUSSION

The measurement of BMD in women is an important aspect to assess bone health and to predict the occurrence of osteoporosis before the clinical disease sets in. As per current recommendation all persons aged more than 65 years should undergo yearly BMD assessment [10]. After achieving menopause the risk of osteoporosis upraises exponentially in each decade [11]. Loss of oestrogen receptors is accountable for accelerated bone loss after menopause. Unfortunately, oestrogen replacement therapy is currently not indicated for sole use in preventing bone loss in postmenopausal women [12]. Proper diet is also very much required for good bone health. Only vegetable diet is a poor source of vitamin B complex which increases homocysteine level in serum causing accelerated bone loss [13]. Similarly, like the present study, in other studies also it has been cited that women who live on vegetarian diet are prone to develop osteoporosis and fracture risks in their later life [14,15].

Osteoporosis is characterised by the gradual reduction in bone mass as a result of imbalance between bone resorption and osteogenesis.

Characteristic		Study group (n=96)	Control group (n=100)	p-value*
Age (years)		42.5 (20-76)	43.7 (20-77)	0.342
Height (cm)		152.5 (146-164)	153.6 (145-166)	0.259
Waist circumference (cm)		86.5 (76-92)	85.9 (78-95)	0.574
Body mass index (kg/m²)		21.4 (17.8-25.6)	25.6 (20.8-27.5)	<0.05
Parity		2.4 (0-4)	2.2 (0-4)	-
Diet	Vegetarian	58 (60.4%)	32 (32%)	<0.05
	Non vegetarian	38 (39.6%)	68 (68%)	<0.05

www.jcdr.net

[Table/Fig-1]: Baseline demographic characteristics

\*p-value were calculated using for each age group, separately and compared using t-tests and Wilcoxon-Mann-Whitney tests

Risk factors *	Number of patients, n (%)
Smoking	8 (8.3%)
Sedentary lifestyle	42 (43.7%)
Alcohol consumption (more than 20g/day)	4 (4.2%)
Body mass index (kg/m²) less than 18.5	6 (6.2%)
Diabetes mellitus	14 (14.6%)
Liver disease	3 (3.1%)
Hyperthyroidism	2 (2.1%)
Chronic kidney disease	3 (3.1%)
Systemic corticosteroid more than 90 days	8 (8.3%)
Antiepileptic drugs	6 (6.2%)
Antidepressants use	32 (33.3%)

[Table/Fig-2]: Spectrum of risk factors. \* Some women having multiple risk factors

Age groups (years)	Study group (n=96)	Control group (n=100)
20- <30	-1.53±0.17 (n=10)	-0.89±0.15 (n=11)
30- <40	-1.78±0.11 (n=24)	-1.08±0.14 (n=21)
40- <50	-2.69±0.09 (n=28)	-2.06±0.13 (n=33)
50- <60	-2.96±0.19 (n=15)	-2.56±0.13 (n=13)
60- <70	-2.95±0.14 (n=11)	-2.88±0.12 (n=15)
70-77	-2.92±0.42 (n=8)	-2.90±0.13 (n=7)

[Table/Fig-3]: Changes of bone mineral density of lumber spine according to age groups.

Age groups (years)	Study group (n=96) Control group (n=	
20- <30	-1.57±0.19 (n=10)	-0.82±0.15(n=11)
30- <40	-1.89±0.13 (n=24)	-0.99±0.15 (n=21)
40- <50	-2.77±0.17 (n=28)	-1.97±0.13 (n=33)
50- <60	-2.92±0.07 (n=15)	-2.52±0.11 (n=13)
60- <70	-2.91±0.23 (n=11)	-2.83±0.10 (n=15)
70-77	-2.97+0.32 (n=8)	-2.86+0.12 (n=7)

 [Table/Fig-4]: Changes of bone mineral density of hip joints according to age groups.

 ± Standard Deviation

Presence of risk factors is responsible for faster resorption of bone mass. Metabolic derangements cause suppression of bone formation by increasing proinflammatory markers like TNF-a, IL-6 and decreasing the serum insulin, Insulin like Growth Factor (IGF-1) which promote for bone formation [16]. CKD is another important matter of concern in respect with bone mass loss. Hyperphosphatemia, hypocalcaemia and increased Parathormone (PTH) level are the main causative factors for developing osteoporosis in CKD patients. Bone care is an important issue in managing the CKD patients as depicted by Kidney Disease Improving Global Outcomes (KDIGO) of National Kidney Foundation (NKF) [17]. CLD is also a risk factor for osteoporosis. Dysregulation between bone formation and bone resorption occurs in CLD due to deficiency of vitamin K, IGF-1.

www.jcdr.net

More over there is deficiency of 25-hydroxy cholecalciferol because of impaired hydroxylation of Vitamin D in the liver [18]. In the present study also, diabetes mellitus, CLD, thyroid dysfunction and CKD has been found as medical risk factors for developing osteoporosis. Prolong corticosteroid use in cumulative dose stimulates bone mass loss by increased apoptosis of osteocyte, decreased VEGF, and increased 11-beta HSD 1 (hydroxy steroid dehydrogenase) activity [19]. Functional disorders like mood disorders, anxiety disorders, manic depression etc., and use of antidepressants in this context often contribute for low BMD and osteoporosis in later life. Selective Serotonin Receptor Inhibitors (SSRIs) and Tricyclic Antidepressants (TCAs) alter serotonin receptor transport system (5-HTT) and thereby increase osteoclastic activities, apoptosis of osteoblast. Additionally, these drugs have sedative effects which may cause fall and fracture of the patients [20]. Antiepileptic drugs are known as inducer of cytochrome P-450 enzyme system and catabolise vitamin D. Deficiency of vitamin D is responsible for developing osteoporosis [21].

Detection of risk factors is important for predicting future development of osteoporosis. Presence of risk factors either single or multiple is responsible for accelerated bone loss. Even without changes in bone mass the BMD may decreases and it can subsequently increases the fracture risks [22]. Study on individual risk factor and the extent of effect individually on BMD is very difficult and often patients present with multiple risk factors. Menopause is known as onset for developing osteoporosis, but even premenopausal are osteoporotic without any significant symptoms. Risk factors play a pivot role in this regard. Osteopenia in presence of risk factor develops a long time ago before menopause and they become osteoporotic much earlier even a decade before menopause. Diagnosis of osteopenia in women is important in respect to her bone health [23]. Preventive interventions by antiresorptive agents (bisphosphonates, SERMs etc.,) along with calcium, vitamin D supplementation are beneficial in delaying the onset of osteoporosis [24]. Use of bisphosphonste since early life for prolong period may predispose to development of osteonecrosis of jaw [25].

### LIMITATION

The above study was done in a small set of study population as a pilot study. Prospective cohort study in the same population group would be a better study model. Considering the logistic and constrain of time present study was a cross-sectional study.

### CONCLUSION

Clinical risk factors of osteoporosis are important tool for preventing bone loss. Assessments of BMD as well as evaluation of risk factors are similarly important in respect with the bone health. Larger prospective cohort study in this regard will be helpful for conclusion.

#### REFERENCES

- Kanis JA, Compston J, Cooper C, Hernlund E, Ivergård M, Johansson H, et al. The burden of fractures in the European Union in 2010. Osteoporos Int. 2012;23:57.
   Deart Iversi A. Deartalaid J. (Sergel and Sergel and Serg
- [2] Doosti Irani A, Poorolajal J, Khalilian AR, Esmailnasab N, Cheraghi N. Prevalence of osteoporosis in Iran: A meta-analysis. J Res Med Sci. 2013;18:759-66.

- [3] Bernabei R, Martone AM, Ortolani E, Landi F, Marzetti E. Screening, diagnosis and treatment of osteoporosis: a brief review. Clin Cases Miner Bone Metab 2014;11(3):201-07.
- [4] Albanese CV, De Terlizzi F, Passariello R. Quantitative ultrasound of the phalanges and DXA of the lumbar spine and proximal femur in evaluating the risk of osteoporotic vertebral fracture in postmenopausal women. Radiol Med. 2011;116:92-101.
- [5] Kanis, J.A., on behalf of the World Health Organization Scientific Group. Assessment of osteoporosis at the primary health-care level. In: Technical report. WHO Collaborating Centre, University of Sheffield, UK; 2008.
- [6] Baim S, Leslie WD. Assessment of fracture risk. Curr Osteoporos Rep. 2012;10:28-41.
- [7] Gimigliano F, Moretti A, Riccio I, Letizia MG, Gimigliano R, Iolascon G. Classification of functioning and assessment of fracture risk of a large Italian osteoporotic population. The physiatric approach to osteoporosis project. Eur J Phys Rehabil Med. 2015;51(5):529-38.
- [8] Isanejad M, Mursu J, Sirola J, Kroger H, Rikkonen T, Marjo T, et al. Journal of Nutritional Science. 2015;4(41):1-8.
- [9] Population based reference standards of peak bone mineral density of Indian males and females: An ICMR multicenter task force study 2010.
- [10] Sharma U, Stevermer JJ. Bisphosphonate therapy: When not to monitor BMD. Hickner J, ed. The Journal of Family Practice. 2009;58(11):594-96.
- [11] Mitra AK, Fernandez GR. Latin America and the Caribbean: assessment of the advances in public health for the achievement of the millennium development goals. Int J Environ Res Public Health. 2010;7(5):2238-55.
- [12] The North American Menopause Society. The 2012 Hormone Therapy Position Statement of The North American Menopause Society. Menopause (New York, NY). 2012;19(3):257-71.
- [13] Compston J, Cooper A, Cooper C, Gittoes N, Gregson C, Harvey N, et al. UK clinical guideline for the prevention and treatment of osteoporosis. Archives of Osteoporosis. 2017;12(1):43.
- [14] Liu N, Zeng F, Zhang K, Tang Z. A community-based cross-sectional study for relationship of frequency of vegetables intake and osteoporosis in a Chinese postmenopausal women sample. BMC Womens Health. 2016;16:28.
- [15] Tucker KL. Vegetarian diets and bone status. Am J Clin Nutr. 2014;100(1): 329S-35S.
- [16] Wong SK, Chin K-Y, Suhaimi FH, Ahmad F, Ima-Nirwana S. The relationship between metabolic syndrome and osteoporosis: a review. Nutrients. 2016;8(6):347.
- [17] Kazama JJ, Iwasaki Y, Fukagawa M. Uremic osteoporosis. Kidney International Supplements. 2013;3(5):446-50.
- [18] Handzlik-Orlik G, Holecki M, Wilczyński K, Duława J. Osteoporosis in liver disease: pathogenesis and management. Therapeutic Advances in Endocrinology and Metabolism. 2016;7(3):128-35.
- [19] Weinstein RS. Glucocorticoid-Induced Osteoporosis and Osteonecrosis. Endocrinology and metabolism clinics of North America. 2012;41(3):595-611.
- [20] Diem SJ, Blackwell TL, Stone KL, Cauley JA, Hillier TA, Haney EM, et al. Use of antidepressant medications and risk of fracture in older women. Calcified tissue international. 2011; 88(6):476-484.
- [21] Carbone LD, Johnson KC, Robbins J, Larson JC, Curb JD, Watson K, et al. Antiepileptic drug use, falls, fractures, and bmd in postmenopausal women: findings from the Women's Health Initiative (WHI). Journal of Bone and Mineral Research. 2010;25(4):873-81.
- [22] Luo Y. Bone mineral density averaged over a region of interest on femur is affected by age-related change of bone geometry. Osteoporos Int. 2018 Mar 5. doi: 10.1007/s00198-018-4461-65.
- [23] Nayak S, Edwards DL, Saleh AA, Greenspan SL. Systematic review and meta-analysis of the performance of clinical risk assessment instruments for screening for osteoporosis or low bone density. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2015; 26(5):1543-54.
- [24] Gallagher JC, Tella SH. Prevention and treatment of postmenopausal osteoporosis. The Journal of Steroid Biochemistry and Molecular Biology. 2014;142:155-70.
- [25] Kim KM, Rhee Y, Kwon Y-D, Kwon T-G, Lee JK, Kim D-Y. Medication related osteonecrosis of the jaw: 2015 position statement of the korean society for bone and mineral research and the Korean association of oral and maxillofacial surgeons. Journal of Bone Metabolism. 2015;22(4):151-65.

#### PARTICULARS OF CONTRIBUTORS:

- 1. Assistant Professor, Department of Obstetrics and Gynaecology, College of Medicine and J.N.M. Hospital, West Bengal University of Health Sciences Kalyani, West Bengal, India.
- Associate Professor, Department of Surgery, College of Medicine and J.N.M. Hospital, West Bengal University of Health Sciences, Kalyani, West Bengal, India.
   Associate Professor, Department of Obstetrics and Gynaecology, College of Medicine and J.N.M. Hospital, West Bengal University of Health Sciences, Kalyani, West Bengal, India.
- Associate Professor, Department of Obstetrics and Gynaecology, College of Medicine and J.N.M. Hospital, West Bengal University of Health Sciences, Kalyani, West Bengal, India.

#### NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Subikas Biswas

Village Santinagar, Post Office Bengal Enamel, District North 24 PG, Barrackpore-743122, West Bengal, India. E-mail: drsubikasbiswas@gmail.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: Oct 13, 2017 Date of Peer Review: Jan 05, 2018 Date of Acceptance: Jun 02, 2018 Date of Publishing: Jul 01, 2018