



STUDY OF BONE MINERAL DENSITY IN PATIENTS OF CARCINOMA BREAST UNDERGOING CHEMOTHERAPY AT CIMS BILASPUR

Medical Science

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ABSTRACT

Background: Breast cancer is the most common cancer and the leading cause of cancer-related deaths among women worldwide. The annual global incidence of breast cancer is estimated to be >1.3 million cases and approximately 465,000 women die of this disease every year. Osteoporosis is a common chronic problem in postmenopausal women that increases the risk for spinal compression fractures and fractures of the femoral neck, causing life-threatening complications. Cancer-induced osteoporosis is a long-term complication associated with cancer therapy that can directly or indirectly affect bone metabolism.

Objective: To estimate the bone mineral density (BMD) before and after the treatment in patients of carcinoma breast

Material & Method: This prospective clinical study involves 27 histopathologically proven cases of carcinoma breast patients which were conducted during October 2017 to August 2018 to estimate the bone mineral density (BMD) before and after the treatment in patients of carcinoma breast. The categorical clinical characteristics between the two treatments are compared using chi-square test.

Result: in this study the Majority of the patients had stage IIIB and IIB disease 12 out of 27(44.4%) patients presented with IIIB disease, 9 out of 27(33.3%) belongs to stage IIB, 4 out of 27 (14.8) were in IIIA, 3 patients out of 27(11.1%) had IIIC disease. The BMD measured at lumbar region included L1 to L4 vertebrae with population matched T-scores and Z-scores. In all 27 patients, the mean BMD at L1, L2, L3 and L4 were 0.885, 0.923, 0.995 and 1.00 gm/cm² respectively. Similarly, among patients completing treatment, mean BMD at L1, L2, L3 and L4 were 0.843, 0.810, 0.867 and 0.911 gm/cm² respectively. The total lumbar spine BMD (L1-L4) was 0.912 ± 0.141 gm/cm² in all 27 patients, whereas it was 0.812±0.879 gm/cm² in patients completing treatment. The maximum BMD value was at L3 (1.90gm/cm²) and minimum value was at L1 (0.641 gm/cm²). The mean lumbar spine BMD values were observed slightly higher among total patients at all sites i.e. L1, L2, L3, L4 and L1-L4, compared to the completed treatment group.

Conclusion: In our study we found that most of the patients with newly diagnosed carcinoma breast had pre-existing osteopenia and osteoporosis, at both Lumbar Spine and Hip regions. The maximum BMD value was at L3 (1.90gm/cm²) and minimum value was at L1 (0.641 gm/cm²). In Hip region the maximum BMD value was found at wards (1.19gm/cm²) and minimum value was at Trochanter (1.0 gm/cm²). In patients completing chemo-radiotherapy, majority of the premenopausal patients were osteopenic, whereas majority of the postmenopausal patients were osteoporotic.

KEYWORDS

Osteoporosis, Bone Mineral Density, Bone Resorption

INTRODUCTION

Breast cancer is the most common cancer and the leading cause of cancer-related deaths among women worldwide.^[1] The annual global incidence of breast cancer is estimated to be >1.3 million cases and approximately 465,000 women die of this disease every year. Advances in technologies for early diagnosis and therapies for breast cancer have substantially improved survival and clinical outcomes in recent years, especially in US and other developed countries.^[2] Breast cancer significantly influences the women's health and is assuming greater importance in the developing countries due to the rising incidence, delay in presentation and dismal outcome.^[3] Osteoporosis is a systemic disease with low bone mass and micro architectural changes that compromises bone strength leading to skeletal fragility and fracture. With increase in life expectancy, osteoporosis is one of the major and serious public health problems and common cause of morbidity and mortality in postmenopausal women and men above 60 years.^[4] A WHO study group has defined osteoporosis as a BMD <2.5 standard deviations below the young adult men.^[5] Patients with a BMD between 1 and 2.5 standard deviations below the young adult mean are classified as having low bone mass, or osteopenia. Osteoporosis is a common chronic problem in postmenopausal women that increases the risk for spinal compression fractures and fractures of the femoral neck, causing life-threatening complications.^[6] Bone mineral densitometry is considered as the gold standard in the diagnosis of osteoporosis. Dual-energy X-ray absorptiometry (DEXA) is precise, accurate, involves exposure to only low doses of X-rays and allows measurement of bones of clinical interest (lumbar spine, proximal femur). Cancer treatment induces bone loss, which causes bone fragility and an increased susceptibility to fractures. Osteoporosis is one of the problems that have been identified with increasing frequency in patients with cancer.^[7] Bone loss in women treated for cancer occurs more rapidly and tends to be more severe compared with the normal age-related bone loss.^[8] Thus, there is a scope for evaluating the bone mineral density in carcinoma breast patients undergoing chemo radiotherapy by measuring BMD.

OBJECTIVE

To estimate and compare the bone mineral density (BMD) in patients with carcinoma breast before and after treatment.

MATERIAL & METHODS

The present prospective clinical study involving 27 patients of carcinoma breast was conducted during October 2017 to August 2018 in the Department of Radiotherapy, in collaboration with the Department of Community Medicine, Chhattisgarh Institute of Medical Sciences, CIMS Bilaspur, Chhattisgarh.

Inclusion criteria:

The patients taken up for the study were required to meet the following criteria.

- Cytologically and histopathologically proven cases of carcinoma breast.
- Premenopausal/postmenopausal women.
- Age more than 25 years and less than 50 years.
- ECOG performance score of 0 or 1.
- Patient with normal liver function test, renal function test and haematological parameters.

Patient with normal electrocardiogram DEXA scan was done to measure bone mineral density in all the patients before start of treatment. The post therapy DEXA scan was done 8-12 months after completion of treatment.

DEXA Scan

Bone mineral density was measured using Dual Energy X-ray absorptiometry (DEXA by GE Medical System Lunar DPX-NT) before start of treatment. Patients underwent both a L1-L4 anteroposterior Lumbar Spine and a Right Hip DEXA study. The DEXA study was done by one observer blinded to the patient's condition.

The bone densities of four regions in the proximal femur (Neck, Ward

triangle, Trochanter and Shaft regions) and of four lumbar vertebrae regions (L1, L2, L3, and L4) were measured by DEXA using the Quantitative Digital Radiography, and the results were expressed as g/cm². The mean BMD for the hip and lumbar regions was calculated using the scanner software. The output data were expressed as T scores and Z scores, determined according to the standard World Health Organization criteria.

WHO Definition of osteoporosis and osteopenia:

Normal = T-score at or above -1.0 SD.
 Osteopenia = T-score between -1.0 and -2.5 SD.
 Osteoporosis = T-score at or below -2.5 SD.

T-score stands for young adult BMD with reference to a standard population aged 20-40 years.

Z-score stands for age matched BMD for a population matched for age and weight 25-100 kg.

Statistically 68% of repeat scans fall within 1 SD (0.030 g/cm² for AP spine and 0.016 g/cm² for right femur).

STATISTICAL ANALYSIS:

In this study, the categorical clinical characteristics between the two treatments are compared using chi-square test. For continuous variables, mean and median values were compared between the groups using the t-test; Pearson Coefficient was used to derive the association between two variables. The comparison between treatment arms were done using log-rank test. A p-value of <0.05 was taken as significant. Data are analysed using the statistical software SPSS for windows (version 19.0).

FOLLOW UP

After completion of treatment, patients were followed up on a monthly basis in the department of Radiotherapy. A minimum of 3 monthly follow up per patient was recorded. They were assessed for loco-regional recurrence and /or distant metastasis by clinical examination and/or by necessary investigations.

RESULTS

The present prospective study was carried out on 27 histopathologically proven cases of Carcinoma Breast during the period October 2017 to August 2018. All patients were evaluated with a detailed history, clinical examination, haematological and radiological investigations. In addition, DEXA scan was done in all patients. 3 patients defaulted either before or during treatment and 3 patients expired during treatment. Hence, only 21 patients completed chemotherapy, and all investigations were repeated during the follow up period.

The results were recorded as per the proforma.

Age

21 out of 27 patients (77.7%) among all patients completed chemotherapy and follow-up on time were in range of 34-50 yrs. And 3 out of 27 patients (11%) who expired after first measurement were in the range of 40-48 yrs. And 3 patients out of 27 (11%) who defaulted in follow-up were in range of 34-40 yrs. mean age were 44±4.9 yrs in all patients completing treatment. From among the 27 patients, the youngest patient was 34 years old and oldest was 50 years of age. (Table-1)

Table -1 Age wise Distribution of Patients

Age Groups (years)	All Patients Nos. (%) (n=27)	Patients Completing treatment Nos. (%) (n=21)
31-40	8 (29.6)	6 (28.5)
41-50	19 (70.3)	15 (71.4)
Mean ± S.D.	43.8±4.9	44±4.9
Minimum	34yrs	35yrs
Maximum	50yrs	50yrs

Menopausal Status

21 patients (77.7%) among all 27 patients were postmenopausal and rest 6 patients (22.2%) were premenopausal. In patients completing treatment and follow-up, 18 out of 21 patients (85.7%) were postmenopausal and the rest 3 patients (14.2%) were premenopausal. (Table-2)

Table -2 Menopausal Status of the patients

Menopausal Status	All Patients Nos. (%) (n=27)	Patients completing treatment Nos. (%) (n=21)
Premenopausal	6 (22.2)	3 (14.2)
Postmenopausal	21 (77.7)	18 (85.7)

TNM

Majority of the patients had stage IIIB and IIB disease. 12 patients out of 27(44.4%) presented with IIIB disease, 9 out of 27(33.3%) belongs to stage IIB, 4 out of 27 (14.8) were in IIIA, 3 patients out of 27(11.1%) had IIIC disease. (Table-3)

Table-:3 Distribution of Patients according to TNM Stage

TNM Stage	All Patients Nos. (%) (n=27)	Patients completing treatment Nos. (%) (n=21)
IIIB	12 (44.4)	13 (61.9)
IIB	9 (33.3)	5(23.8)
IIIA	4 (14.8)	3 (14.2)
IIIC	3(11.1)	2 (9.5)

Bone Mineral Density (BMD) at Lumbar Spine

The BMD measured at lumbar region included L1 to L4 vertebrae with population matched T-scores and Z-scores. In all 27 patients, the mean BMD at L1, L2, L3 and L4 were 0.885, 0.923, 0.995 and 1.00 gm/cm² respectively. Similarly, among patients completing treatment, mean BMD at L1, L2, L3 and L4 were 0.843, 0.810, 0.867 and 0.911 gm/cm² respectively. The total lumbar spine BMD (L1-L4) was 0.912 ± 0.141 gm/cm² in all 27 patients, whereas it was 0.812±0.879 gm/cm² in patients completing treatment. The maximum BMD value was at L3 (1.90gm/cm²) and minimum value was at L1 (0.641 gm/cm²). The mean lumbar spine BMD values were observed slightly higher among total patients at all sites i.e. L1, L2, L3, L4 and L1-L4, compared to the completed treatment group.

Table-: 4 Lumbar Spine BMD distribution

Site	In All patients (n=27)				In patients completing treatment (n=21)			
	Max	Min	Mean	SD	Max	Min	Mean	SD
L1	1.168	0.641	0.885	0.136	1.168	0.641	0.843	0.112
L2	1.244	0.467	0.923	0.158	1.206	0.467	0.810	0.116
L3	1.907	0.504	0.995	0.239	1.177	0.504	0.867	0.147
L4	1.897	0.479	1.00	0.225	1.283	0.479	0.911	0.131
L1-L4	1.167	0.489	0.912	0.141	1.167	0.489	0.857	0.141
Z-Score	-0.2	-3.0	-1.5	.879	-0.2	-3.0	-0.912	0.879
T-Score	0.5	-3.6	-1.6	1.20	0.5	-3.6	-1.57	1.17

Bone Mineral Density (BMD) at Right Hip

The BMD measured at Right Hip region included Neck, Ward triangle, Trochanter and Shaft region with population matched T-scores and Z-scores. Among all 27 patients, the mean BMD measurements at Neck, Ward triangle, Trochanter and Shaft were 0.862, 0.718, 0.732 and 1.111 gm/cm², respectively. Similarly, in patients completing treatment, the mean BMD measurements at Neck, Ward triangle, Trochanter and Shaft were 0.838, 0.690, 0.694 and 1.09 gm/cm², respectively. The mean total Right Hip BMD (L1-L4) was 0.870±0.146gm/cm² in all 27 patients, whereas it was 0.876±0.116 gm/cm² in patients completing treatment. The maximum BMD value was at ward triangles (1.19gm/cm²) and minimum value was at Trochanter (1.0 gm/cm²). The mean right hip BMD values were observed slightly higher among total patients as compared to the patients completing treatment in all sites, i.e. Shaft, Neck, Ward triangle, Trochanter and Total Hip. (Table-5)

Table-:5 Right Hip BMD distributions

Site	In All patients (n=27)				In patients completing treatment (n=21)			
	Max	Min	Mean	SD	Max	Min	Mean	SD
Neck	1.17	0.647	0.862	0.126	1.02	0.649	0.838	0.108
Ward triangle	1.19	0.487	0.718	0.157	0.952	0.506	0.690	0.129
Trochanter	1.03	0.516	0.732	0.127	0.865	0.566	0.694	0.084
Shaft	1.67	0.676	1.11	0.231	1.30	0.800	1.09	0.138
Total Hip	1.17	0.524	0.870	0.146	1.09	0.668	0.876	0.116
Z-Score	2.0	-2.3	-0.17	0.900	1.10	-2.7	-0.34	0.994
T-Score	2.3	-2.7	-0.48	1.04	1.0	-2.1	-0.59	0.874

DISCUSSION

In the present study 21 out of 27 patients (77.7%) who completed treatment were in range of age 34-50 yrs. 3 out of 27 (11%) who expired after first BMD measurement were in the age range of 40-48 yrs. And 3 patients out of 27 (11%) who defaulted in follow-up were in the range of 34-40 yrs mean age was 44 ± 4.9 yrs in patients completing treatment. 21 patients (77.7%) among all 27 patients were postmenopausal and rest 6 patients (22.2%) were premenopausal. In patients completing treatment, 19 out of 21 patients (90.4%) were postmenopausal and the rest 2 patients (9.5%) were premenopausal. Majority of the patients had stage IIIB and IIB. 12 patients out of 27(44.4%) presented with IIIB disease, 9 out of 27(33.3%) had stage IIB, 4 out of 27 (14.8) were in IIIA, 3 patients out of 27(11.1%) were at the time of presentation had IIIC.

The peak value of BMD measured in Indian women has been 0.588 g/cm² at age 35 years and 0.602 g/cm² in men at age 42 years.^[9] There were statistically significant differences in BMD in women and men across all age groups. Out of 200 women studied by Aggarwal N et al.^[10] 106 were found to have low BMD (osteopenia and osteoporosis). The prevalence of low BMD was found in more than half of the study population (53%). The difference in BMD values of Indian and Western females in the study by Ranu Patni (2010)^[11] was found to be significant, with a *P*-value <0.01 in all age groups. In a retrospective analysis of BMD by DEXA scan of Hip and Spine in 1,282 asymptomatic Indian women in age group 40-60 years, Acharya et al. (2010)^[12] determined the average BMD of spine and hip to be 0.89 (SD 0.14) gm/cm² and 0.85gm/cm²(SD 0.15), respectively. The correlation between BMD and age was negative. Spine DEXA was found to be more significant than hip DEXA (*P* value<0.0001) for osteoporosis assessment. Only 35% of the population had normal bone density with 18.41% prevalence of osteoporosis with WHO criteria and the remaining 47% had osteopenia.

In the present study BMD measured at lumbar region included L1 to L4 vertebrae with population matched T-scores and Z-scores. In all 27 patients, the mean BMD at L1, L2, L3 and L4 were 0.751, 0.775, 0.827 and 0.836 gm/cm² respectively. Similarly, among patients completing treatment, mean BMD at L1, L2, L3 and L4 were 0.766, 0.787, 0.839 and 0.846 gm/cm², respectively. The total lumbar spine BMD (L1-L4) was 0.803 ± 0.175 gm/cm² in all 74 patients, whereas it was 0.814 ± 0.183 gm/cm² in patients completing treatment. The maximum BMD value was at L3 (1.674gm/cm²) and minimum value was at L2 (0.467gm/cm²). The mean lumbar spine BMD values were observed slightly higher among completed treatment group as compared to the total patients at all sites, i.e. L1, L2, L3, L4 and L1-L4.

The baseline BMD results showed that majority of the patients had pre-existing osteopenia and osteoporosis. As compared to premenopausal, postmenopausal patients had significantly lower BMD values. A very high significant difference (*p*=0.001) in mean Lumbar Spine and Right Hip BMD was found between premenopausal and postmenopausal patients at all sub-sites including BMD T-scores. There was a generalized fall in bone mineral density in premenopausal to postmenopausal group as measured both in Hip DEXA (0.889 ± 0.09 vs 0.873 ± 0.135 gm/cm²) and Spine DEXA (1.013 ± 0.74 vs 0.900 ± 0.135 gm/cm²) along with consistent rise in number of patients with established osteoporosis. Similar distribution of bone mass was also reported by Acharya et al. (2010),^[12] in the study of 1282 Indian women in age group of 40-60 years.

On a closer study, DEXA scan of spine was found to be more sensitive for picking osteoporosis in majority of the patients as compared to Hip DEXA. Only 10 patients were diagnosed by Hip DEXA as osteopenic or osteoporotic, on the other hand, 17 patients had either osteoporosis or osteoporosis with spine DEXA scan. Acharya et al. (2010).^[12] In a study by Shapiro PL et al. (2001)^[13] of 49 premenopausal women with stage I or II breast cancer receiving adjuvant chemotherapy, 35 experienced ovarian failures, defined as more than 3 months of amenorrhea. In the group as a whole, regardless of menopausal status at 1 year, median decreases in BMD of 6.3% in the lumbar spine, 3.9% in the femoral neck, and 3.8% in the trochanter were observed. In those who experienced ovarian failure, median decreases in BMD of 7.7% in the lumbar spine and 4.6% in the femoral neck were reported. In another study (Kanis et al. 1999),^[14] the annual incidence of vertebral fracture was compared in women on follow-up after primary breast cancer treatment to general population and was found to be nearly five times greater (*P*<0.0001), In women with recurrent disease it was more than 20 times greater (*P*<0.0001).

CONCLUSION

A history of chemo-radiotherapy for breast cancer was associated with decreased bone mineral density (BMD) in postmenopausal women. DEXA is the most widely used method for BMD measurements because of its lower cost, accuracy and lower radiation exposure. In our study we found that most of the patients with newly diagnosed carcinoma breast had pre-existing osteopenia and osteoporosis, at both Lumbar Spine and Hip regions. The maximum BMD value was at L3 (1.90gm/cm²) and minimum value was at L1 (0.641 gm/cm²). In Hip region the maximum BMD value was found at wards (1.19gm/cm²) and minimum value was at Trochanter (1.0 gm/cm²). In patients completing chemo-radiotherapy, majority of the premenopausal patients were osteopenic, whereas majority of the postmenopausal patients were osteoporotic. Highly significant difference was found in mean BMD both at Lumbar Spine and Right Hip regions between premenopausal and postmenopausal patients. Rapidly progressing bone resorption results in worsening of osteoporosis which causes bone fragility and an increased susceptibility to fractures at Lumbar spine and Hip region. Clinicians should be aware of the risk of bone loss, so that such predisposed patients can be screened and treated appropriately to prevent the long-term morbidity and mortality of osteoporosis in these patients.

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