

ORIGINAL ARTICLE

Analysis of BMD and Serum Calcium Level in Patients with or without Bony Metastatic Breast Cancer

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ABSTRACT:

Objective: To analyze bone mineral density (BMD) and serum calcium in patients with and without bony metastatic breast cancer.

Materials and Methods: This descriptive study was conducted in KIRAN Hospital Karachi and Department of Biochemistry, BMSI-JPMC Karachi from March 2011 to March 2012. After approval by BASR of Karachi University 200 diagnosed cases of breast cancer, reproductive and postmenopausal age group females, passing through any stage of cancer, married or unmarried, lactating or non-lactating, having different body mass index, passing through any cycle of chemotherapy and radiotherapy were selected. Consent of patients was taken on a form. Bone scan was done on Siemen E Cam scanner. Intravenous dye 20/mci technetium 99 MDP has been used, to check the bone metastasis in breast cancer patients. Test for Bone Mineral Density was done on Hologic software version 12. Serum calcium levels were checked on Selectra-E- semi auto biochemical analyzer.

Results: 40-49 years group showed highest number of cases of osteoporosis (24%). Bone scan positive patients showed osteopenia (11%) in 40-49 years group. Distribution of subjects with osteopenia (15%) was more common in bone scan negative patients especially in age group of 40-49 years. Serum calcium level was found to be comparatively increased in bone scan positive patients than in bone scan negative patients again in age group 40-49.

Conclusion: In bone scan positive patients osteoporosis and serum calcium were high in comparison to bone scan negative patients with most vulnerable age group being 40-49 years, in diagnosed cases of breast cancer.

Keywords: Breast cancer, Bony metastasis, Bone scan, Bone mineral density, Osteoporosis, Osteopenia, Serum calcium.

INTRODUCTION:

Breast cancer is a big challenge for health in females. It is still growing problem but strenuous efforts for early catch of disease and best treatment as a combine therapy has greatly decreased the associated mortality in metastatic cases. But 5 years survival rate is 25% only¹. Short survival reasons may be the complex and heterogenous mechanism of metastasis influenced by various biological features and site of metastasis. Visceral metastasis has appeared as one of the main cause of

short survival².

A retrospective analysis of circulating cell tumor, there deposition and progress of disease has been done for the assessment of survival and as technique to monitor the disease. It has found that circulating tumor cells before treatment strongly correlate with visceral disease and direction of their spread (circulating tumor cells as early predictors of metastatic spread in breast cancer patients with limited metastatic dissemination)³. Bone scintigraphy is proved as a common procedure to extract the knowledge of tumor metastasis, extent of burden and associated survival.^{4,5,6} Bone scan is a prognostic indicator and used as imaging biomarker in cancers, showing bony metastatic tendency^{7,8,9}. The relationship between localized bone scan measurement with age and survival have found no correlation and localized bone scan imaging value was (P= 0.1), however result of regional bone scanning was significant (P<0.05)¹⁰. George have found direct relationship of higher BMD of total body to high lean mass and FM (Fat mass) of body¹¹

Victims of breast cancer often suffer in skeletal weakening. As research has proved, non- pathological hip fractures are more common and at early on set in postmenopausal women. The risk of fall is 15% and 55% for fracture of hip.^{12,13,14} Bone is the most common site of distant metastases from breast cancer and is the first affected site in a substantial proportion of women with advanced breast cancer.¹⁵ In advance stages of cancer showing tendency to spread to bones are associated with severe skeletal illness and complications until they received Bis- phosphonates.¹⁶ Hypercalcemia was commonly found in patients with squamous cell lung cancer, breast cancer, kidney cancers and some blood cancers. The main cause of this hypercalcemia was found to be bone destruction in almost 80% of cases. Hypercalcemia was also found in cancer metastasis

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but the main cause might be reduced parathyroid and related hormones¹⁷. Baker has documented resorptive changes and osteoporosis in relation to RANKL gene, ostoproteogen and AMG 162 and have found decreased calcium and phosphorous levels in patients with cancers resting AMG 162 as antiresorptive factor (Ant Rank L monoclonal antibody).¹⁸ Present study was designed to find out the frequency of bone mineral density (BMD) and serum calcium in patients with and without bony metastatic breast cancer

MATERIALS AND METHODS:

Selection of patients: After approval by BASR of Karachi University 200 diagnosed cases of breast cancer were selected for this descriptive study. The study was conducted in the KIRAN Hospital Karachi, Biochemistry Department of BMSI-JPMC Karachi from March 2011 to March 2012. Reproductive and postmenopausal age group females, passing through any stage of cancer, married or unmarried, lactating or non-lactating, having different body mass index, passing through any cycle of chemotherapy and radiotherapy were included in the study. A memorandum of understanding (MOR) was signed by authorized persons of University of Karachi and KIRAN hospital. Willingness (signature) of every patient was taken on patients form.

Bone scan: Bone scan was done on Siemen E Cam scanner with accessories. Intravenous dye technetium 99 MDP was used. This test helps to see if a cancer has metastasized to bones and is useful because it provides a picture of the entire skeleton. For this purpose, 20/mci (dose) of radioactive material (technetium 99) was injected into a vein (intravenously or IV). The substance settles in areas of damaged bone throughout the entire skeleton over the course of a couple of hours. (Six hours to twenty four hours). Patient was made to lie down on a table for about 30 minutes while a special camera detected the radioactivity and created a picture of the skeleton (Figure 1).

Figure: 1
Bone scan film



Skeleton after dispersion of radioactive dye, affected areas appeared as dark spots. (With the permission of Kiran Hospital Karachi.)

Biophysical parameters BMD: was performed with DEXA technique using discovery-w (HOLOGIC), P/A spines and left hip images were acquired, the data was analyzed by HOLOGIC Software version 12. Result

of BMD (computerized software) was interpreted by calculating the area of image in square centimeter, bone mineral content, bone mineral density, T and Z score. T score is used for patients between 40- 65 age group and Z score is used for patients < 40 years and above 65 years age group. T score is < -1, BMD is normal. T score is in between 1.1- 2.4, patient is osteopenic. T score is > 2.5, patient is osteoporotic. Z score is < -2.0, BMD is normal. Z score is >2.0, patient is osteoporotic.

Biochemical parameter serum calcium: Serum Calcium was determined by in vitro test for the quantitative determination of calcium in human serum and plasma on Roche automated clinical chemistry analyzer. Kit Cat. No. 14862 Ecoline.²⁰ Sample collection: samples, 3ml, were collected in heparinized syringe. Reagents: were Reagent 1 composed of Imidazole buffer 100mmol/L PH 6.5. 1,8-dihydroxy-3,6,2-7- and Reagent 2 composed of naphthalene-bis dibenzene arsonic acid (Aesenzazo 111) 120mmol/L.

All (except CA15-3) were done on Selectra-E, XL semi auto biochemical analyzer. Vital Scientific and diagnostic Machine, Netherland, Holand latest model by ROCH (Figure 2).

Figure: 2
Selectra-E XL semi auto- biochemical analyzer



RESULTS:

In patients with positive bone scan, bone mineral density was measured. Age group of 40-49 years showed highest number of cases of osteoporosis. Higher frequency of osteoporosis showed in age group of 60-69 years. Age group 50-59 years and above 70 showed the same frequency of osteoporosis but comparatively less as compared to age group 40-49 and 60-69 years (Table 1) Bone scan positive patients showed osteopenia in age group 40-49 years at same frequency. Distribution of subjects with osteopenia was more common in bone scan negative patients especially in age group of 40-49 years as compared to osteoporosis. 24% cases had osteoporosis on BMD in five bone scan were significantly high as compared to 9% negative BS (P<0.01) (Table 2). Serum calcium level was found to be comparatively increased in bone scan positive patients than in bone scan negative patients, especially in age group 40-49 and above. Comparison of serum calcium levels among different age groups of positive and negative bone scan was found to be insignificant except in age group 40-49 years where serum calcium level was less in subjects

with negative bone scan as compared to positive bone scan (Table 3 & Figure 3)

Table: 1
Comparison of age with bone scanning

Age in years	Bone scanning		P-value
	Positive (n=100)	Negative (n=100)	
Under 30	8	5	0.732
30-39	20	21	
40-49	32	35	
50-59	22	27	
60-69	12	9	
70 & above	6	3	

** Statistically Significant p<0.01

Table: 2
Biophysical parameters in bone scanning positive and negative cases

Bone Mineral Density	Bone scanning		P-value
	Positive (n=100)	Negative (n=100)	
Normal	65	76	0.088
Osteoporosis	24**	9	0.004
Osteopenia	11	15	0.400

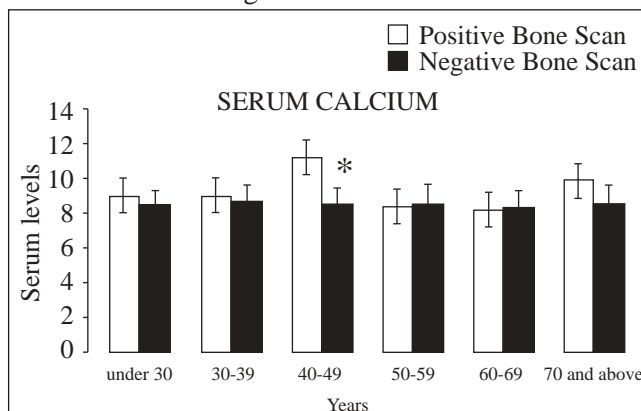
** Statistically Significant p<0.01

Table: 3
Biochemical parameter in bone scanning positive and negative cases

	Bone scanning (Positive) (n=100)			Bone scanning (Negative) (n=100)			P-value
	Mean	S.D	SEM	Mean	S.D	SEM	
Serum Calcium	11.3	21.09	2.13	8.5	0.67	0.07	0.191

** Statistically significant p<0.01

Figure: 3
Serum calcium levels in subjects with positive and negative bone scan



Values represented as means ± SD. Statistically significant difference from patients with positive bone scan following student t- test were not found

DISCUSSION:

The most frequent cancer all around the world is the breast cancer. Breast cancer in Asian population causes nearly 40,000 deaths per year. Every 1 in 9 of Pakistani women will suffer from breast cancer at some stage in their lives²⁰. Pakistan faces a high burden of breast cancer disease with late presentation. In this study 81% patients were diagnosed in late stage. Another study also showed the late presentation in advanced stages III and IV, in 71% patients²¹. The causes of late presentation were social, self-neglect, fear of surgery, and financial constraints etc.²²

Previous research has established the percentage of breast cancer metastasis to bones approximately 80% or more especially in cases with advance stages of carcinoma and the destructive osteolysis. Many other bone related complications are associated with metastasis and osteolysis. In spite of this patients with breast cancer and bone metastasis may survive for many years.^{23,24,25}

Houssani has proved that PET scan, MRI and CT scan may enhanced the accuracy of diagnosis of bone metastasis of cancer but the accuracy was only some degree greater than bone scan (BS), cost is very high of above mentioned tests as compared to bone scan and little evidence support application of these tests for diagnosis of bone metastasis. Still BS is preferred as first line of imaging.²⁶

Our study showed significant relationship of bone scan, breast cancer and bone mineral density (P<0.04) in cases of breast cancer with bone metastasis for osteoporosis. That is evident of high risk of osteoporosis and morbidity in number of cases with positive bone scan of breast cancer. Osteopenia was seen more commonly in patients of breast cancer with negative bone scan. George has compared skeletal weakening and no pathological fractures in postmenopausal women without cancer and found increase incidence of non pathological hip fractures and osteoporosis at early age onset in patients with breast cancer. Disentangling the body weight bone mineral density association among breast cancer survivors. An examination of the independent roles of lean mass and fat mass.¹¹

Fraenkel has provided the additional information based on research to find out the association of BMD and risk of breast cancer and found a significant risk of breast cancer development and low survival rate in cases with low BMD and high BMI as compared to women with low BMI and high BMD.²⁷

Serum calcium level in patients with bony metastatic breast cancer and related osteopenia was non-significant in our study. Serum calcium levels were almost normal in most of cases in positive bone scan but levels were found to be decreased in negative bone scan in perimenopausal women. Rowan has found out the relation between breast cancer in postmenopausal women and VitD₃ level but result was significant.²⁸ In another study of 718 patients with bony metastatic breast cancer, hypercalcemia is indicated as a skeletal complication. Medium time for spread to skeletal areas and first relapse was determined to be 11 months. Survival was longer

in cases with the diagnosis of bony metastasis as compared to other site of metastasis.¹⁷

CONCLUSION:

In bone scan positive patients osteoporosis and serum calcium were high in comparison to bone scan negative patients with most vulnerable age group being 40-49 years. There is a strong relationship seen between breast cancer, bone scan and bone mineral density. In Patients with bony metastatic breast cancer, osteoporosis is more common as a skeletal complication. Perimenopausal age group of breast cancer is more prone to osteopenia even without bone metastasis. Serum calcium level is independent of bone metastasis and was found comparatively less in negative bone scan patients.

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