

## Original Research Article

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# Hypercalcemia in advanced cases of carcinoma breast: hospital based study

Arifa Almas<sup>1\*</sup>

Department of Surgery, IIMSR Medical College, Warudi, Jalna, Maharashtra, India

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**\*Correspondence:**

Dr. Arifa Almas,

E-mail: drarifaalmas@gmail.com

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## ABSTRACT

**Background:** Hypercalcemia due to cancer is an indicator of poor prognosis, and has been often found to be associated with the disseminated form of disease. Present study describes the serum and urinary calcium levels among the advanced cases of carcinoma breast with respect to stage of disease, presence of osseous metastases and also before and after treatment. It is a hospital based study done at Government Medical College, Jabalpur in Madhya Pradesh state of India.

**Methods:** The present hospital-based and descriptive study was done at the Surgery Department of Government Medical College at Jabalpur in Madhya Pradesh, India. 50 patients with confirmed breast cancer diagnosis were enrolled in the study. Serum calcium was estimated by Clark and Collip's method. Urinary calcium was estimated by Sulkowitch method. Serum and urinary calcium levels were compared with respect to stage of disease, presence of osseous metastases and also before and after treatment.

**Results:** Out of 50 cases, raised level of serum calcium and positive urinary calcium was observed in all except 2 cases of stage II disease. Serum calcium levels were found to be higher in stage III and stage IV disease and the differences were found to be statistically significant. Serum calcium level was slightly more raised in cases with osseous metastasis (mean 14.4 mg%) in comparison with cases with non-osseous metastasis (mean 13.3 mg%) however, the difference was statistically not significant. Follow up data after treatment was available for 34 cases. After treatment, reduction in serum and urinary calcium levels was noted in all stages of disease and the decrease in serum calcium levels in stage III and stage IV disease was found to be statistically significant.

**Conclusions:** Hypercalcemia was noticed in almost all cases of advanced carcinoma breast and the serum calcium levels were significantly higher in stage III and stage IV of the disease. There was a significant decrease in serum calcium levels after treatment of the disease which was predominantly surgical treatment alone or in combination with radiotherapy or chemotherapy.

**Keywords:** Breast cancer, Osseous metastases, Serum calcium, Urinary calcium

## INTRODUCTION

Hypercalcemia associated with cancer is the commonest form of hypercalcemia noted among hospital admitted patients with an overall prevalence ranging from 10% to 30% among the cancer patients. Also, among the subjects with advanced stages of cancer, around one tenth

develops hypercalcemia which represents the commonest cause of mortality in several patients with cancer. Hypercalcemia due to cancer is an indicator of poor prognosis, and has been often found to be associated with the disseminated form of disease. Severe form of hypercalcemia if left untreated can be fatal, but proper treatment can provide relief of many symptoms and also

positively impact the quality of life of the patient.<sup>1-3</sup> Present study describes the serum and urinary calcium levels among the advanced cases of carcinoma breast with respect to stage of disease, presence of osseous metastases and also before and after treatment. It is a hospital based study done at Government Medical College, Jabalpur in Madhya Pradesh state of India.

## METHODS

The present hospital-based and descriptive study was done at the Surgery Department of Government Medical College at Jabalpur in Madhya Pradesh, India during the years 1990 - 91. 50 patients with confirmed breast cancer diagnosis were enrolled in the study. Written informed consent was obtained from the participants. Detailed clinical examination was done along with relevant investigations and available records were analyzed. Serum calcium was estimated by Clark and Collip's method. Serum calcium level of 9 - 11 mg% was considered normal. Urinary calcium was estimated by Sulkowitch method. Serum and urinary calcium levels were compared with respect to stage of disease, presence of osseous metastases and also before and after treatment. Treatment of breast cancer was done depending on stage of cancer by surgical management, chemotherapy, radiotherapy or combination therapy. Chi square test and student's t test were used for analysis. P-value of less than 0.05 was considered as statistically significant.

## RESULTS

Age of patients ranged from 30 years to 65 years. With respect to stage of disease, Stage II patients were 16%,

stage III were 54% and stage IV were 30%. There were 6 cases of osseous metastasis. Among them, 2 cases with skull metastasis and 4 cases with spine involvement were found. Out of 50 cases, raised level of serum calcium and positive urinary calcium was observed in all except 2 cases of stage II disease.

**Table 1: Serum and urinary calcium levels in different stages of malignancy.**

Stage	Serum calcium mean (mg%)	Serum calcium range (mg%)	Urinary calcium
Stage - II	11.7	9 to 13.4	Negative to +
Stage - III	13.9	11.8 to 15	+ to ++
Stage - IV	15.8	12.3 to 16.6	++

Serum calcium levels were found to be higher in stage III and stage IV disease and the differences were found to be statistically significant. Serum calcium level was slightly more raised in cases with osseous metastasis (mean 14.4 mg %) in comparison with cases with non-osseous metastasis (mean 13.3 mg%) however, the difference was statistically not significant (Table 1-4).

Out of 50 cases, follow up data after treatment was available for 34 cases. Reduction in serum and urinary calcium levels was noted in all stages of disease after management by modalities described in Table 3. After treatment, decrease in serum calcium levels in stage III and stage IV disease was found to be statistically significant.

**Table 2: Serum and urinary calcium levels in osseous metastasis and non-osseous metastasis.**

Site of metastasis	Serum calcium range (mg%)	Serum calcium mean (mg%)	Urinary calcium
<b>Osseous</b>			
Skull	15.2 to 16.6	14.4	++
Spine	12.6 to 14.4		++
<b>Non-osseous</b>			
Lymph node	11 to 14.6	13.3	+ to ++
Liver	12 to 14.8		++
Lung	12 to 14.4		+ to ++

**Table 3: Different modalities of treatment in different stages of malignancy.**

Stage	Number of cases	Radiotherapy (RT)	Chemotherapy (CT)	Surgery	Surgery + CT	Surgery + RT
Stage - II	8	-	-	6	2	-
Stage - III	27	-	-	6	13	8
Stage - IV	15	6	2	--	2	5
<b>Total</b>	<b>50</b>	<b>6</b>	<b>2</b>		<b>12</b>	<b>17</b>
						<b>13</b>

**Table 4: Serum calcium and urinary calcium before and after treatment in different stages of malignancy (total number of cases with follow up: 34).**

Stage	Number of cases	Before treatment			After treatment		
		Serum calcium range (mg%)	Serum calcium mean (mg%)	Urinary calcium	Serum calcium range (mg%)	Serum calcium mean (mg%)	Urinary calcium
Stage - II	8	9 to 13.4	11.7	Neg to +	9 to 10.2	9.8	Neg
Stage - III	19	11.8 to 15	13.9	+	11 to 12.2	11.2	+
Stage - IV	7	12.3 to 16.6	15.8	++	11.8 to 12.8	12.3	+

## DISCUSSION

In our study hypercalcemia was noticed in almost all cases of advanced carcinoma breast and the serum calcium levels were significantly higher in stage III and stage IV of the disease. Presence of hypercalcemia in association with cancer is considered to be contributed by: local factors like osteolytic hypercalcemia due to bone resorption at sites of bone metastasis; humoral factors like tumours secreting parathormone related protein; enzyme secretions causing increase in absorption of calcium by converting 25-OH vitamin D to 1, 25-dihydroxy vitamin D and ectopic parathormone secretion.<sup>5</sup>

In our study, serum calcium levels were found to be higher in stage III and stage IV disease and the differences were found to be statistically significant. Serum calcium level was slightly more raised in cases with osseous metastasis (mean 14.4 mg%) in comparison with cases with non-osseous metastasis (mean 13.3 mg%) however, the difference was statistically not significant.

Breast cancer is among the most frequent malignancies found to be associated with high serum calcium levels. Usually, this hypercalcemia is caused by osteolytic metastases signalling a poor prognosis. However, it has been reported that a significant proportion of the cancer breast patients have high serum calcium levels even if there are no osseous metastasis.<sup>6-9</sup>

Lumachi et al have recently reviewed literature related to cancer related hypercalcemia and mentioned that 'increased osteoclast-mediated bone resorption induced by release of tumor-derived mediators is the primary cause of cancer induced hypercalcemia (CIH).<sup>2</sup> Parathyroid hormone-related protein (PTHrP) is the main mediator of interactions between cancer cells and the osteoclasts, it also activates osteoblasts to produce receptor activator of nuclear factor- $\kappa$  ligand (RANKL) and osteoclast precursors, with subsequent bone osteolysis. They further described the two different therapeutic approaches for treating CIH i.e. to increase the urinary excretion of calcium, or to inhibit osteoclastic bone resorption, RANKL or the action of PTHrP. In patients with CIH, restoration of renal function is the first step of therapy; renal function is often impaired due to dehydration. They highlighted that bisphosphonates

administration is at present the main-stay of treatment, while calcitonin, gallium nitrate and mithramycin have limited activity and several side-effects. Also, it was mentioned that Anti-RANKL therapy (denosumab) and antibodies against PTHrP are promising therapies for management of CIH'.

Limitations of our study include smaller sample size and only serum and urinary calcium levels were obtained. Data regarding parathormone levels could not be collected. Further studies are needed to better understand mechanisms behind hypercalcemia and explore management options for the same.

## CONCLUSION

Hypercalcemia was noticed in almost all cases of advanced carcinoma breast and the serum calcium levels were significantly higher in stage III and stage IV of the disease. There was a significant decrease in serum calcium levels after treatment of the disease which was predominantly surgical treatment alone or in combination with radiotherapy or chemotherapy.

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## REFERENCES

1. Seccareccia D. Cancer-related hypercalcemia. Canadian Family Physician. 2010;56(3):244-6.
2. Lumachi F, Brunello A, Roma A, Basso U. Medical treatment of malignancy-associated hypercalcemia. Curr Med Chem. 2008;15(4):415-21.
3. Bower M, Cox S. Endocrine and metabolic complications of advanced cancer. In: Doyle D, Hanks G, Cherny NI, Calman K, editors. Oxford textbook of palliative medicine. 3<sup>rd</sup> edition. New York, NY:Oxford University Press. 2004:688-90.
4. Clark EP, Collip JB. A study of the Tisdall method for the determination of blood serum calcium with a suggested modification. J Biol Chem. 1925;25:461.
5. American cancer society. Cancer Facts and Figures 2008. Atlanta: American Cancer Society; 2008.

6. Rao V, Chaukar D, Cruz AK. Hypercalcemia and treated breast cancers: the diagnostic dilemma. *J Can Res Ther.* 2009;5:46-8.
7. Mundy GR, Guise TA. Hypercalcemia of malignancy. *Am J Med.* 1997;103:134-45.
8. Marcocci C, Borsari S, Pardi E, Dipollina G, Giacomelli T, Pinchera A, et al. Familial hypocalciuric hypercalcemia in a woman with metastatic breast cancer: a case report of mistaken identity. *J Clin Endocrinol Metab.* 2003;88:5132-6.
9. Conroy S, Malley B. Hypercalcemia in cancer. *BMJ.* 2005;331:954.

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