

**Original Research Article**

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DETERMINATION OF SERUM CALCIUM AND ALBUMIN LEVELS IN PATIENTS WITH CANCER OF THE BREAST, CERVIX AND PROSTATE AT PARIRENYATWA GROUP OF HOSPITALS, RADIOTHERAPY CLINIC HARARE, ZIMBABWEAR DZORO¹, DT ZHOU^{1, 2*}

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ABSTRACT: Cancers of the breast, cervix and prostate are the commonest malignancies in Zimbabwe. Monitoring changes in serum calcium levels could assist in management of complications of these cancers; as they sometimes involve calcium, so-called paraneoplastic hypercalcemias. The objective of this study was to determine serum calcium and albumin levels in patients with cancer of the breast, cervix and prostate. Total serum calcium and albumin levels were determined in samples of 30 breast cancer patients, 30 cervical cancer patients and 30 patients with prostate cancer. Samples were analysed using automated colometric methods. Serum calcium levels were significantly higher than normal in all three groups. Prostate cancer patients have the highest prevalence of elevated serum calcium (46.7%) and cervical cancer patients have the lowest prevalence (30%). The monitoring of hypercalcemia may be of biochemical and clinical relevance to cancer patients in our setting, as it was highly prevalent in prostate, breast and cervical patients studied.

KEYWORDS: Cancer, calcium, albumin, hypercalcemia, Zimbabwe

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1.INTRODUCTION

Cancer is a disease caused by an uncontrolled division of abnormal cells in a part of the body resulting in malignant growth and tumor[1]. Cancer is now the second leading cause of mortality and morbidity in sub-Saharan Africa after acquired immunodeficiency syndrome (AIDS)[2]. The condition is associated with many complications which include immunosuppression that increases susceptibility to infection. In addition, cancer may cause ectopic hormones synthesis disturbing the homeostasis of the body[3].The Global Burden of Cancer (GLOBOCAN) study showed that lung cancer followed by breast cancer are the most prevalent cancers, globally and the two are responsible for the highest mortality rates amongst all known cancers [4,5]. In our context, the incidence of cancer in Zimbabwe has increased from 19.1 % in 2006 to 23.9% in 2013 [5]. The rise in cancer patients has been attributed to the AIDS pandemic as well as other sexually transmitted infections especially those caused by human papilloma virus (HPV) which is the commonest aetiological factor for cervical cancer-a leading cause of cancer deaths in Zimbabwe [5,6,7]. Cancer is associated with the derangement of the body's physiological functions, alterations in homeostasis and production of biochemical metabolites [3]. Neoplasms can alter homeostasis through production of endocrine factors resulting in humoral hypercalcemia of malignancy; this is relatively common in multiple myeloma, breast cancer, lung cancer and prostate cancer [1, 3]. Hypercalcemia in cancer patients is usually due to the secretion of parathyroid hormone related protein (PTHrP) by the tumor. To a lesser extent it is caused by the tumor conversion of calcidiol to calcitriol-the active form of vitamin D [8]. In addition, hypercalcemia, can be caused by primary and tertiary hyperthyroidism, poor renal excretion and limited nephritic and intestinal reabsorption or as a complication of haematological malignancies or solid tumors in the absence of bone metastasis [1, 9, 10].Results from a Nigerian study indicated 30% prevalence of hypercalcemia and a significant increase in calcium and phosphates amongst breast cancer patients though clinical symptoms of hypercalcemia may be mistaken for malignancy symptoms- [1,11,12]. An Italian study reported hypercalcemia as the most common life- threatening metabolic disorder associated with cancer [13]. In Japan paraneoplastic hypercalcemia was more common in haematological malignancies. The Japanese study and related literature also report that the increase in the levels serum calcium with time suggests that it could be used in monitoring treatment and disease progress in resource-poor setting [13, 14]. We hypothesised that patients with cancer of the breast, cervix and prostate are at risk of paraneoplastic related hypercalcemia. The aim of this study was to contribute towards existing knowledge on calcium related complications of cancer and improve their management in Zimbabwe.

2. MATERIALS AND METHODS

Study design, study site and study population

The current cross sectional study was conducted at Parirenyatwa Group of Hospitals, the largest referral hospital in Harare, Zimbabwe. Cancer patients attending the Radiotherapy Clinic (RTC) at PGH were enrolled into the study. The patients were enrolled on the basis of being aged 18 years and older, whether female or male with cancer.

Ethical considerations

The study was ethically cleared by the Joint Research Ethics Committee of the University of Zimbabwe College of Health Sciences and Parirenyatwa Group of Hospitals (JREC) after they were satisfied that the study would be carried out in accordance with recommendations in the Declaration of Helsinki. Patients were approached at the clinic and those who agreed to participate were recruited after giving written informed consent.

Sample collection

Patients were bled once, when they came for review or radiotherapy treatment, samples were collected into plain tubes and serum were frozen and thawed only once for analysis.

Sample analysis and data analysis

Serum samples were thawed to room temperature and were analysed on the Mindray BS 120 Chemistry analyser (Mindray Biomedical Electronics Company, Shenzhen, China) [15]. Serum calcium was measured using Arsenazo III method and albumin was measured using the Bromo-cresol green (BCG) method [15]. Data was analysed using Stata® 10.0 (Texas, USA) and compared using analysis of variance (ANOVA) method of distinct component division.

3. RESULTS AND DISCUSSION

Thirty patients each with breast cancer, cervical cancer and prostate cancer, respectively were recruited, 56 (62.2%) were females. Of all the breast cancer patients, four (13.3%) were males. The youngest patient had cervical cancer whilst the oldest had prostate cancer. The mean (SD) age for breast cancer patients was 43 (11.8) years, that of cervical cancer patients was 47 (11.9) years while that for prostate cancer patients was 68 (13.2) years. Cervical and breast cancer both have an early onset, which may be due to predisposition in the case of breast cancer and sexually transmitted virus in the case of cervical cancer. Prostate cancer had a later onset and was common in older men in their late fifties. In general there was no difference in the mean calcium of both female and male cancer patients. However, males had slightly higher values in both calcium and albumin with a borderline statistical significance for albumin ($p=0.05$). Generally all the mean albumin levels across the age groups were within the normal reference range. The lowest albumin and calcium levels were found in patients less than 30 years whilst those over 60 had slightly elevated albumin levels.

Out of a total of 90 patients, 36 (40%) had serum calcium levels above 2.56mmol/L hence were considered to be hypercalcemic. The calcium levels were not different across all cancer patients ($P=0.101$), whereas the albumin levels showed statistically significant difference ($P=0.033$) (Table 1). Mean albumin level was significantly higher among prostate cancer patients compared to cervical cancer patients, ($p=0.028$). However, mean albumin levels of breast cancer patients and cervical cancer patients were not different ($p=0.745$). Likewise, there was no difference in mean albumin levels between those with prostate cancer and breast cancer, ($p=0.417$). Out of a total of 90 patients, 36 (40%) had serum calcium levels above 2.56mmol/L hence were considered to be hypercalcemic. 43.3% of breast cancer patients, 30% of those with cervical cancer and 46.7% of patients with prostate cancer had hypercalcemia.

Table 1: Comparison of serum calcium and albumin by cancer type using ANOVA

Analytes	Breast cancer	Cervical cancer	Prostate cancer	P
	Mean (SD)	Mean (SD)	Mean (SD)	
Albumin (g/L)	43.00 (6.1)	41.18(6.14)	45.33(6.0)	0.033
Ca (mmol/L)	2.57(0.24)	2.46(0.19)	2.55(0.22)	0.101

ANOVA=Analysis of Variance, Ca= Calcium, SD= Standard deviation, Significant P value<0.05

DISCUSSION

Mean (SD) age for cervical cancer patients was 47(11.9) years, which is in agreement with data from GLOBOCAN study, where median age of diagnosis for cervical cancer is 47 years [4]. The GLOBOCAN study also shows that there is significantly higher incidence among women of lower socioeconomic class as well as women with a history of early sexual debut. However, our Zimbabwean study did not employ the use of questionnaires that could tell the demographic characteristic of the patients. The Nigerian Calabar study showed that breast cancer patients had 30% prevalence of hypercalcemia [16]. Prevalence of hypercalcemia was even higher in this Zimbabwean study (43.3%). Therefore, there is evidence that breast cancer results in elevated calcium levels, in a large proportion of this Zimbabwean group of breast cancer patients, in agreement with literature [1, 13, 17]. There was significant elevation of calcium in breast cancer patients in Nigeria [16] similar to that observed in the breast cancer patients, with regards to calcium, in the current study. Approximately 30% of those with cervical cancer had hypercalcemia and 46.7% of patients with prostate cancer had hypercalcemia. This is in agreement with a 2008 study from Schwartz et al [18], but in contrast to report by Vassilopoulou-Sellin et al. (1993) who reported low incidence in patients referred to a comprehensive cancer center in the USA [19] and Jick et al who reported consistently lower prevalence in UK cancer patients over 10 years (2003-2012) [20]. For example, of the 7076 prostate cancer patients in UK databases, annual hypercalcemia prevalence increased from 0.28% to 0.48% between 2003 and 2015.

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4. CONCLUSION

From our study, it can be concluded that paraneoplastic hypercalcemia is common in patients with cancer of the breast, cervix and prostate at Parirenyatwa Radiotherapy Clinic. Therefore, regular monitoring of serum calcium and albumin levels is important in order to decrease mortality and morbidity that could be contributed by hypercalcemia of malignancies.

LIMITATIONS

In this study, samples were analysed only once due to limited resources. Ideally, hypercalcemia is confirmed by repeated determination of the analyte because there can be misleading alterations consequent of prolonged venous stasis at the time of blood collection.

RECOMMENDATIONS

Further studies with a larger population size would give a good statistical representation of the population. The grading and staging of the cancer patients would help to describe the characteristics of the cancer progression in relation to the paraneoplastic hypercalcemia. Patients will have to be tested for other conditions that result in transient hypercalcemia like primary hyperthyroidism. In addition, measurement of PTHrP, as well as other hormone analytes like PTH, calcitonin and vitamin D can confirm paraneoplastic hypercalcemia. Furthermore, the serum calcium reference values of our population need to be determined together with collection of demographic and clinical data of participants in further studies.

CONFLICT OF INTEREST

The authors have no conflict of interest.

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