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Assessment of Bone minerals and Alkaline phosphatase activity in Breast cancer subjects

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Abstract: *Breast cancer is a disease condition that is associated with alterations in the body's physiological homeostasis. Bone metastases are common in advanced cancer and cause considerable morbidity and mortality. The study aimed to assess the serum levels of alkaline phosphatase activity and the bone minerals in breast cancer. A total of 80 subjects within the ages of 20-65 years were investigated (40 breast cancer subjects and 40 age-matched apparently healthy female subjects as controls). Serum calcium was estimated using calcium kit from Randox Laboratories, inorganic phosphate and magnesium were estimated using kits from Biosystems while the estimation of serum alkaline phosphatase activity was done using King Armstrong's method. The serum total calcium and serum alkaline phosphatase activity were significantly increased (P<0.05) while serum magnesium was significantly decreased (P<0.05) in breast cancer subjects compared with the control subjects. There was no significant increase in serum inorganic phosphate of the breast cancer subjects compared with the control subjects. There was no significant difference in the mean serum levels of the bone minerals and ALP activity between the breast cancer subjects on chemotherapy and those not on chemotherapy. It was concluded that regular laboratory assessment of serum levels of bone minerals and ALP activity should be carried out on breast cancer patients to avoid bone associated disorders.*

Keywords*: Alkaline phosphatase, breast cancer, calcium, inorganic phosphate, magnesium .*

I. Introduction

Breast cancer is a disease condition that is associated with alterations in the body's physiological homeostasis. It is the leading cause of cancer death among females accounting for 23% (1.38 million) of the total cancer cases and 14% (458,400) of the cancer deaths in women[1]. It has also been demonstrated that more than 1100 women between the ages 17 and 85years have been diagnosed with breast cancer in Nigeria since 1995[2]. Although tremendous progress in the treatment of breast cancer has been achieved during past decade, it is still the principal cause of cancer death among women worldwide[1,3]. The majority of breast cancer patients die not because of the tumor at the primary site, but due to (metastases) at secondary sites[4]. Bone metastases are common in advanced cancer and cause considerable morbidity including pain, pathological fractures, hypercalcemia and increasing disability[5]. Non surgical treatment options such as hormonal therapy, chemotherapy, radiation, bisphosphonate therapy, are undoubtedly improving outcomes for women with breast cancer; however these therapies also carry significant skeletal side effects[6]. For instance, adjuvant hormonal treatments such as aromatase inhibitors that disrupt the estrogen-skeletal axis have the potential to cause decreased bone mineral density[7]**.** Similarly chemotherapy often induces primary ovarian failure in premenopausal women, resulting in decreased levels of circulating estrogen and subsequent osteopenia, in both cases, women receiving these therapies are at an increased risk for the development of osteoporosis and skeletal fracture[8]. Furthermore, it was stated that osteoporosis is common in women with breast cancer who receive chemotherapy, hormone therapy, or surgical castration, because these treatments induce bone loss[9]. Since most chemotherapy in clinical practice is given as a combination of several agents and chemotherapy is often combined with steroid therapy, they will contribute to bone loss[10]. Thus, the study set to assess the serum levels of alkaline phosphatase activity and the bone minerals in female subjects with breast cancer as this could help in monitoring to prevent bone mineral loss and other complications that may arise as a result of derangement in the levels of these parameters.

II. Materials And Methods

The study was conducted among female participants who have been both clinically and histopathologically proven to have breast cancer. Age-matched females with no previous history of breast cancer or cancer related diseases served as control. A total of 80 subjects within the ages of 20-65 years (40 breast cancer subjects and 40 age-matched apparently healthy female subjects as controls) were recruited by random sampling technique. Informed consent was obtained from the participants before recruitment into the study. Those on chemotherapy received four courses of combination therapy of Cyclophosphamide, 500 mg/m^2; Adriamycin, 50 mg/m^2 and 5-Fluorouracil, mg/m^2. The drugs were given at intervals of three weeks. Five millimeters of whole blood was collected from the participants into plain containers using the standard venipuncture technique. The serum was separated from the clotted sample after centrifugation and stored frozen until analysis was carried out.

Serum calcium was estimated using calcium kit from Randox Laboratories limited, Inorganic phosphate and magnesium were estimated using kits from Biosystem Inc. while the estimation of serum alkaline phosphatase activity was done using King Armstrong's method.

Statistical method

The statistical analysis was performed using the Statistical Package for Social Sciences (SPSS program) version 17 at a significance level of 0.05. The means and standard deviations (SD) were calculated for each parameter and the differences in the means for each parameter were compared using student's t- test.

III. Results

The mean serum levels of the bone minerals and ALP activity studied are represented in table 1. The mean serum levels of calcium, magnesium inorganic phosphate and alkaline phosphatase activity in the breast cancer subjects were 2.58 ± 0.27mmol/l, 0.49 ± 0.10mmol/l, 0.55 ± 0.19mmol/l and 96.95 ± 28.37U/L respectively. The mean serum levels of calcium, inorganic phosphate, magnesium and ALP activity in control subjects were 2.26 ± 0.16 mmol/l, 0.70 ± 0.06mmol/l, 0.54 ± 0.10mmol/l and 46.10 ± 16.48 respectively.

Table 2 shows the mean serum levels of calcium, magnesium inorganic phosphate and alkaline phosphatase activity in the breast cancer subjects on chemotherapy and those not on chemotherapy. The results of those on chemotherapy were 2.26 ± 0.15mmol/l, 0.50 ± 0.11mmol/l, 0.59 ± 0.22mmol/l and 94.31 ± 28.95U/L respectively. The mean serum levels of calcium, inorganic phosphate, magnesium and ALP activity in breast cancer subjects not on chemotherapy were 2.25 ± 0.19mmol/l, 0.50 ± 0.10mmol/l, 0.57 ± 0.21mmol/l and 101.86 ± 27.64 respectively.

Table 1: Bone Minerals And Alkaline Phosphatase Activity In Breast Cancer Subjects.

Serum Parameters	Breast cancer subjects (n=40)	Control subjects (n=40)	T value	P value
Calcium (mmol/l)	2.58 ± 0.27	2.26 ± 0.16	6.31	0.00*
Magnesium (mmol/l)	0.49 ± 0.10	0.70 ± 0.06	−10.98	0.00*
Inorganic phosphate (mmol/l)	0.55 ± 0.19	0.54 ± 0.10	0.27	0.78
Alkaline phosphatase (mmol/l)	96.95 ± 28.37	46.10 ± 16.48	9.79	0.00*

***** =Significant at $p<0.05$

Table 2: Effect Of Chemotherapy On Bone Minerals And Alkaline Phosphatase Activity In Breast Cancer Subjects

Serum Parameters	Chemotherapy (n=26)	No Chemotherapy (n=14)	T value	P value
Calcium (mmol/l)	2.26 ± 0.15	2.25 ± 0.19	0.078	0.938
Magnesium (mmol/l)	0.50 ± 0.11	0.50 ± 0.10	0.001	0.99
Inorganic phosphate (mmol/l)	0.59 ± 0.22	0.57± 0.21	0.27	0.78
Alkaline phosphatase (mmol/l)	94.31 ± 28.95	101.86 ± 27.64	-0.79	0.42

IV. Discussion

The mean total serum calcium level of breast cancer subjects was found to be significantly higher than in the control subjects. This finding is in line with a similar research which showed that serum calcium levels were significantly higher in the breast cancer than in the control group[11]. The increased serum calcium levels

(hypercalcemia) in breast cancer have been attributed in part to osteolytic bone metastases and this account for about 20%-30% of the hypercalcemia cases[12]. There was no significant increase in the mean serum level of inorganic phosphate in breast cancer subjects compared with control subjects. This finding is also in line with the research that demonstrated that there was no significant difference in mean levels of inorganic phosphate of both groups[11]. However, the mean serum magnesium levels of breast cancer subjects were significantly lower than that of control group. Magnesium is essential for DNA duplication and repair but magnesium deficiency favors DNA mutations leading to carcinogenesis[13]. The mean serum ALP activity of breast cancer subjects was significantly higher than those of control group. This finding also agrees with the works in which ALP activity was significantly higher in female breast cancer subjects when compared with control subjects[11,14,15] as well as the work in which ALP activity was evaluated in pre and post-operative breast cancer patients[16]. The increased activity of this enzyme seen in breast cancer subjects may be due to osteolytic bone metastases in breast cancer leading to increased osteoclastic activity and bone resorption. There was no statistically significant difference in the mean serum levels of the bone minerals (calcium, magnesium, inorganic phosphate) and ALP activity between the breast cancer subjects on chemotherapy and those not on chemotherapy contrary to the findings of some researchers[9,10]. It has been reported that chemotherapy can have both direct and indirect effects on the bone microenvironment ultimately leading to decreased bone mineral density[17].

V. Conclusion

This work reveals that women with breast cancer have increased calcium with low magnesium levels and increased ALP activity than in apparently healthy women. The alteration of these biochemical parameters is an indication that their measurement may be useful tools in monitoring treatment and disease progression in breast cancer subjects. We therefore suggest regular laboratory assessments of serum levels of bone minerals and ALP activity in breast cancer subjects to avoid bone associated disorders especially as the disease progresses.

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