ORIGINAL RESEARCH PAPER

Biochemistry

EVALUATION OF SERUM ALKALINE PHOSPHATASE IN DIFFERENT MALIGNANT DISEASES AND ITS CORRELATION WITH SERUM CALCIUM AND PHOSPHOROUS.

KEY WORDS:

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ABSTRACT

Introduction: Alkaline phosphatase (ALP) is present in a number of tissues including liver, bone, intestine and placenta. Hypercalcemia is a common finding among different malignancies. Around 10-20% of patients with malignancy develop Hypercalcemia at some point of disease. It is usually found to be associated with Hypophosphatemia as metabolisms of both are closely interrelated.

Aims and Objective: Study of Serum Alkaline Phosphatase, Calcium and Phosphorus levels in different malignant diseases and find out its relation with different malignant diseases.

Methods and Materials: A hospital based case control study was conducted in Deptt. of Biochemistry among 60 patients of various malignant diseases from OPD &wards in MAMC, New Delhi and 60 controls. Serum Alkaline Phosphatase was measured by modified Kind-King method. Serum Phosphate was measured by modified Metol method and Calcium was measured by O -cresophthalein Method. Absorbance was measured using colorimeter and analysis was done. **Results:** Mean ALP level in cases was (16.68 ± 2.36) K.A. as compared to controls (8.42 ± 1.88) K.A. which was significantly higher ($p<0.001$). Mean Calcium was (13.08 ± 1.46) mg/dl in cases, which was significantly higher than controls (9.86 ± 0. 48) ($P<0.001$). Mean Phosphorous was (2.82 ± 0.60)mg/dl in cases, which was significantly lower ($P<0.001$) than controls (4.36 ± 0.82).

Conclusion: The present study shows higher levels of S.ALP and Calcium, while S. Phosphorous levels were decreased in malignancies.

INTRODUCTION:

Alkaline phosphatase (ALP) comprises a group of enzymes that catalyze the hydrolysis of phosphate esters in an alkaline environment. (1) Alkaline phosphatase is present in the placenta, ileal mucosa, kidney, bone, and liver. The majority of alkaline phosphatase in serum (more than 80%) is released from liver and bone, and in small amounts from the intestine. The liver is the source in most patients with elevated enzyme levels. Increased osteoblast activity seen in disorders of the bone or normally during periods of growth is the next likely contributor. The influx of placental alkaline phosphatase in the late third trimester contributes to the rise in pregnant women.(2) Disorders that do not primarily involve the liver such as intra-abdominal infections, cholestasis of sepsis, Hodgkin lymphoma, myeloid metaplasia, and osteomyelitis can also cause moderate elevation of serum alkaline phosphatase.

Primary or metastatic cancer raises serum alkaline phosphatase levels by local bile duct obstruction and increasing leakage of the liver isoenzyme. Primary extrahepatic cancer does not necessarily have to involve the liver or the bone; rarely, some tumors can produce their own alkaline phosphatase (Hodgkin lymphoma secreting the Regan isoenzyme) or exert a paraneoplastic effect causing leakage of the hepatic isoenzyme into the circulation (Stauffer syndrome due to renal cell carcinoma. (3,4)

Hypercalcemia is a common finding among different malignancies. Around 10-20% of patients with malignancy develop Hypercalcemia at some point of disease. It is the most common life-threatening metabolic disorder in patients with advanced stage cancers and is a sign of poor prognosis. It usually presents with markedly elevated calcium level and is severely symptomatic. (5) It is usually found to be associated with Hypophosphatemia as metabolisms of both are closely interrelated.

Hypophosphatemia, defined as serum phosphorus 2.5 mg/dL, is a common occurrence in cancer patients and is associated with increased morbidity and mortality. Phosphorus is essential for the normal physiologic function of all cells and its homeostasis is frequently interrupted by cancer and cancer therapy. (6)

AIMS AND OBJECTIVE:

To study Serum Alkaline Phosphatase, Calcium and Phosphorus levels in different malignant diseases and find out its relation with different malignant diseases.

MATERIAL AND METHODS

A case control study was conducted in Department of Biochemistry, Maulana Azad Medical College, New Delhi. Sixty patients diagnosed with various malignant diseases from OPD & wards and 60 controls between the age group of 18 to 70 years fulfilling inclusion criteria were selected from various wards of Maulana Azad Medical College and associated Lok Nayak Hospital from November 2018 to August 2021.

All patients were examined thoroughly. Anthropometric and Laboratory data was collected and results were statistically analysed. All the patients and their relatives were informed about the study in their vernacular language. Written consent was taken. Clinical examination and all the relevant investigations were performed.

Under all aseptic conditions 5 ml of blood in plain vial was collected from each individual.it was allowed to clot and serum was separated by centrifuging at 3000 rpm for 20 minutes. Serum Alkaline Phosphatase was measured by modified Kind-King method. Serum Phosphate was measured by modified Metol method and Calcium was measured by O - Cresophthalein Method. Absorbance was measured using colorimeter and analysis was done.

Results were tabulated and subjected to statistical analysis using SPSS and represented in the form of bar diagrams and pie charts as and where required.

Inclusion Criteria

1 Histologically or clinically proven cases of various religion, tribes, casts and language were selected for the study.

2 The cases were selected irrespective of the age, sex and duration of the disease.

Exclusion Criteria

1. Those who had already received palliative therapy
2. Patients suffering from conditions causing hypercalcemia (i.e.- Primary hyperparathyroidism, pagets disease of bone, tuberculosis, histoplasmosis)
3. Chronic liver disease patients

Sixty age and sex matched apparently healthy individuals were selected as control group irrespective of their casts or religion.

RESULTS:

Table - 1

Table 1: Distribution of serum calcium, phosphorous and alkaline phosphatase levels in cases and control groups

Group	Cases (n=60)	Controls (n=60)	P value
Calcium(mg/dl)	13.08 ± 1.46	9.86 ± 0. 48	< 0.001
Phosphorous (mg/dl)	2.82 ± 0.60	4.36 ± 0.82	< 0.001
Alkaline Phosphatase (KA)	16.68 ± 2.36	8.42 ± 1.88	< 0.001

All values expressed in (Mean ± SD)

Table - 2

Table 2: Serum calcium, Phosphorous and Alkaline phosphatase levels in different malignancies

Type	No of cases	Serum calcium (mg/dl)	Serum phosphorous (mg/dl)	Serum alkaline phosphatase ()
Breast	11	13.48 ± 1.86	2.96 ± 0.68	12.86 ± 2.42
Female Genito-urinary tract	11	12.11 ± 1.62	3.28 ± 0.92	13.46 ± 2.72
Male Genito Urinary tract	05	14.68 ± 1.90	2.88 ±0.73	14.60 ± 3.54
G I tract	07	12.42 ± 1.72	2.96 ± 0.82	11.26 ± 3.08
Lungs	10	14.74 ± 2.04	2.42 ±0.58	19.20 ± 4.66
Thyroid	06	11.86 ± 1.44	2.68 ± 0.62	12.68 ± 2.36
Larynx	07	12.68 ± 1.88	3.12 ± 0.80	12.78 ± 2.30
Multiple Myeloma	03	15.96 ± 2.46	2.04 ± 0.36	23.86 ± 5.74

Table -3

Table-3 : Serum calcium levels in different malignant diseases with and without evident bony metastasis

Type	Serum calcium Mean ± SD (Mg/dl)			
	With evident bony metastasis		Without evident bony metastasis	
	No.	Mean ± SD	No.	Mean ± SD
Breast	7	14.86 ± 2.08	4	11.86 ± 0.57
Female Genito-urinary tract	4	13.56 ± 1.87	7	11.09 ± 1.35
Male Genito Urinary tract	3	16.26 ± 2.65	2	12.84 ± 1.42
G I tract	-	-	7	12.42 ± 1.72
Lungs	4	15.62 ± 2.39	6	13.88 ± 1.78
Thyroid	3	12.38 ± 1.98	3	10.58 ± 1.26
Larynx	2	13.42 ± 2.06	5	11.78 ± 1.69
Multiple Myeloma	3	15.96 ± 2.46	-	-

The study group consist of 32 males between age group of 22 to 69 years with an average age of 48 years and 28 females aged between 24 to 62 years with mean age 43 years. Among the 8 different types of malignancies examined maximum no was for female malignancies (i.e., 11 carcinoma breast and 11 female genito-urinary tract) followed by lung carcinoma (n=10). (Table -2).

it was observed that serum alkaline phosphatase levels were significantly higher in cases (16.68 ± 2.36) compared to controls (8.42 ± 1.88). This difference was statistically significant ($p < 0.001$). serum was calcium was also observed to be higher in cases (13.08 ± 1.46) compared to controls (9.86 ± 0.48) while serum phosphorous was found to be lower in cases (2.82 ± 0.60) compared to controls (4.36 ± 0.82). both of these were statistically significant. ($p < 0.001$). (Table -1)

Table -2 shows values of all three parameters in different malignancies. Highest mean Serum ALP (23.86 ± 5.74), Calcium (15.96 ± 2.46 mg/dl) and lowest mean serum phosphorous (2.04 ± 0.36 mg/dl) were found in Multiple Myeloma. While Lowest mean ALP (11.26 ± 3.08) was found in GI tract malignancy, Lowest mean calcium (11.86 ± 1.44 mg/dl) was found in thyroid malignancy, Highest mean serum phosphorous (3.28 ± 0.92 mg/dl) was found in malignancy of female Genito-Urinary Tract.

Table - 3 compares serum calcium with respect to bony metastasis. In case of evident bony metastasis values were highest (16.26 ± 2.65 mg/dl) in malignancy of male Genito-Urinary Tract and lowest (12.38 ± 1.98 mg/dl) in thyroid malignancies. In cases without evident bony metastasis values were highest (13.88 ± 1.78 mg/dl) in malignancies of lungs while were lowest (10.58 ± 1.26 mg/dl) in thyroid malignancies.

DISCUSSION:

Malignant diseases produce profound biochemical and haematological changes in the body of the hosts. In present study 3 parameters were examined among these.

Hypercalcemia of malignancy is a common finding typically found in patients with advanced stage cancers. The pathophysiology of hypercalcemia of malignancy is mainly through three mechanisms: excessive secretion of parathyroid hormone-related protein (PTHrP), bony metastasis with the release of osteoclast activating factors, and production of 1,25-dihydroxy vitamin D (calcitriol). (7) Major mechanism, accounting for approximately 80% of malignancy-related hypercalcemia, is mediated by the production of PTHrP. PTHrP acts on osteoblasts, leading to enhanced synthesis of RANKL, with subsequent activation of osteoclasts and bone resorption with calcium release into the bloodstream. Increased renal calcium reabsorption is another mechanism through which PTHrP leads to hypercalcemia. Squamous cell cancers, urinary tract cancers (renal cancer and bladder cancer), breast cancer, nonHodgkin's lymphoma, and ovarian cancer account for the majority of malignancies leading to hypercalcemia via PTHrP. (8) It is interesting to note that metastatic breast cancer cells may produce PTHrP locally, without a major increase in serum PTHrP. (9)

Bony metastasis causing the release of osteoclast activating factors contribute to 20% of thecases and are commonly seen in patients with multiple myeloma and solid organ tumors which metastasize to bones such as breast cancer. (7)

n adults, elevations in ALP can be observed in numerous conditions, including pregnancy, congestive heart failure, ulcerative colitis, and bacterial infections. Increased liver ALP level is most frequently observed in hepatobiliary conditions, particularly cholestasis, whereas elevations in bone ALP levels are encountered in pathologies of increased osteoblast activity such as Paget disease or certain cancers that either originate from bone or have spread to bone (10). Most data indicate that the elevation of serum ALP occurs because of the accelerated de novo synthesis of the enzyme and subsequent regurgitation into the serum (11)

Hypophosphatemia is a common disorder in cancer patients that can result from malignancy itself or from its therapy. Poor

intake, transcellular shift, GI and renal loss or RRT can all contribute to this condition. (6) Hypophosphatemia may also be the only manifestation of an occult malignancy. A high index of clinical suspicion can help diagnose such conditions in early stages. Prompt treatment of the cause can correct this biochemical abnormality (12)

CONCLUSION.

The present study shows higher levels of S.ALP and Calcium, while S. Phosphorous levels were decreased in malignancies. The average values of ALP vary depending upon the presence or absence of metastasis. The level was highest in case of multiple myeloma and lowest in malignancies of GI Tract.

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