



## ALKALINE PHOSPHATASE AS A PROGNOSTIC MARKER IN CANCER BREAST PATIENTS IN A TERTIARY CARE HOSPITAL

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### ABSTRACT

**OBJECTIVE:** To estimate the value of Alkaline Phosphatase in cancer breast patients in a tertiary care hospital.

**MATERIAL AND METHODS:** The study was conducted to estimate the value of Serum Alkaline Phosphatase in 50 cancer breast patients and 50 normal patients of same age as a control group.

**RESULTS:** The level of serum Alkaline Phosphatase was significantly increased ( $p < 0.05$ ) in cancer patients compared to the control group.

**CONCLUSION:** There is an increase in serum Alkaline Phosphatase in cancer patients compared to the control group and can be a prognostic markers for the progress of the disease.

**KEYWORDS :** Alkaline Phosphatase, cancer breast, prognostic marker.

### INTRODUCTION

Tumour markers are used for detection of risk, population screening, diagnosis, staging and prognosis of cancers. It can also predict the response to the therapy, the presence of occult metastasis and monitor the course of disease. Various tumour markers have been studied singly or in combination in carcinoma breast. Most of these are high on running costs, in terms of laboratory infrastructure.

In India breast cancer is the second most common cancer in the female population. Although tremendous progress in the treatment of breast cancer has been achieved during past decades, it is still the principal cause of cancer death among women worldwide<sup>[1,2]</sup>.

According to National Cancer Registry Programme in India the frequency of breast cancer prior to 25 years occurred above 50 years of age, but in present day women in the age group of 25-40 years of age has high frequency of breast cancer. Highest incidence of breast cancer is seen in the age 45-49 years. Multiple factors are associated with an increased risk of developing breast cancer; these can be genetic, environmental and histological factors.

Alkaline Phosphatase comprises a group of isoenzymes that catalyses the hydrolysis of phosphate esters in an alkaline environment, generating an organic radical and inorganic phosphate.

Alkaline phosphatase (ALP) is a serum enzyme whose total levels reflect the combined activity of several isoenzymes found in the liver, bone, kidney, and intestinal lining. The skeletal isoenzyme originates in osteoblasts that release large amounts of the enzyme when bone repair activity occurs, for example with bone metastases. In cancer patients, ALP is a sensitive indicator of mild biliary obstruction, thus being a very sensitive indicator of liver progression. In a study conducted by the International Breast Cancer Study Group (IBCSG), ALP, aspartate transaminase (AST) and c-glutamyl transferase (GGT) were examined for their sensitivity in detecting breast cancer recurrence. ALP alone was abnormal in a high proportion of breast cancer patients with bone metastases and/or liver metastases, and was more effective than AST and GGT in distinguishing patients with relapse from those without<sup>[3]</sup>.

Hence Alkaline phosphatase can be a valuable marker in cancer breast. Thus the present study is designed to evaluate the levels of serum Alkaline phosphatase in carcinoma breast and to assess their role and significance. Alkaline phosphatase can also be used as a diagnostic and prognostic marker of

breast cancer in women, therefore helping secondary prevention of breast cancer.

### AIMS AND OBJECTIVES

The main aim of this study is to estimate the value of Alkaline Phosphatase in carcinoma breast in females and normal patients as control group.

### MATERIAL AND METHODS

The study was an observational study conducted on female patients with carcinoma breast admitted in surgical ward at Rajendra Institute of Medical Sciences, Ranchi during the period January 2018-October 2019.

**SAMPLE SIZE:** A total of 100 subjects were taken.

**GROUP A-** Includes 50 patients which were diagnosed with carcinoma breast by tissue diagnosis.

**GROUP B-** Includes 50 controls who were of the same age matched normal healthy individuals.

### INCLUSION CRITERIA

All female diagnosed clinically and histopathologically with carcinoma breast of any age group before treatment and surgery.

### EXCLUSION CRITERIA

Female patients suffering from:  
Tuberculosis, Rheumatic fever, Haemolytic anaemia, Hypertension, Diabetes mellitus, Hepatitis, Jaundice, Pancreatic diseases, Pregnancy or breast feeding, Hormonal therapy, Oral contraceptives, non-smokers, Bone diseases, Cardiac failure, Myocardial infarction, Ulcerative colitis and other malignancies.

### REFERENCE VALUES:

**NORMAL FEMALES**  
20-50 years- 42 - 98 U/L  
≥ 60 years- 53-141 U/L

### METHODOLOGY

Blood was obtained with written consent of each cases and controls and a proper questionnaire was provided. Clinical history was taken from the subjects and examination findings were noted.

Proper physical examination and history was taken along with questionnaire was provided with written consent.

### BIOCHEMICAL EXAMINATION

Serum Alkaline phosphatase was estimated in BECKMAN COULTER AU480.

Detection limit:5-1500 U/L

### Principle:

Serum Alkaline phosphatase activity was determined by measuring the rate of conversion of p-Nitrophenyl phosphate (pNPP) to p-Nitrophenol (pNP) in the presence of magnesium ions and diethanolamine as phosphate acceptor at pH 9.8.

The rate of increase in absorbance due to the formation of pNP is measured at 410/480nm and is directly proportional to the ALP activity in the sample<sup>[4]</sup>.

### Method Of Sample Collection

Patients were instructed for the procedure to be undertaken and to remain calm and compose.

Following safety measures were followed while collecting blood samples:

- Wearing gloves after handling blood.
- Changing gloves after handling of each patient or when contaminated.
- Washing hands frequently.
- Disposal of items in appropriate containers.
- Disposal of needles immediately upon removal from patients.
- Cleaning up any blood spills with a freshly made 10% bleach disinfectant.

Needles of 20 or 22 G Size were used for blood samples. Needles were put in disposable unit immediately after their use. 70% isopropyl alcohol was used in cotton swab to wipe and sterilize the skin.

### Procedure

The antecubital vein of the arm was preferred and used most frequently for collection of blood. First the surface was palpated and the path vein was traced with index figure. Arteries were identified and avoided as they pulsate, are more elastic and having a thick wall. Once the preferred site was selected, gloves were put on. Venepuncture site was cleaned with alcohol preparation, cleansing in a circular fashion. The site was allowed to dry.

The tourniquet was applied 3-4 inches above the selected puncture site. Precaution was taken not to apply tourniquet too tightly. Venepuncture performed with patients arm rested in a comfortable position. Tourniquet was removed as soon as the blood appeared in the syringe. About 5-6 ml of blood was withdrawn. When blood has been collected, a cotton ball or gauze was placed over the site and the needle withdrawn in a smooth and cautious manner so as not to bruise the vein or skin. After withdrawing the needle, gentle pressure was applied to the cotton ball over the puncture site. The patient was asked to apply pressure for 3-5 minutes to prevent oozing of blood from puncture site. Then blood samples were put in appropriate vial.

The serum sample blood was allowed to clot by placing in the rack at room temperature for at least 30 minutes. Then it was centrifuged at 3000 rpm for 10 minutes and serum was separated. The clear serum was then analysed for the estimation of serum Alkaline phosphatase.

### Statistical Method And Data Analysis

Statistical analysis was done using SPSS software. The data was represented by counts, percentage and mean  $\pm$  standard deviation. Statistical analysis of the biochemical tests of serum Alkaline phosphatase was done by unpaired t-test to compare the parameters in carcinoma breast cases and control.

P value of <0.05 was considered statistically significant.

### Observation And Results

The present study is an observational study comprising of 100

patients including 50 cases of carcinoma breast (Group A) and 50 cases of control (Group B) in Rajendra Institute of Medical Sciences, Ranchi during the period January 2018-October 2019.

The general characteristics of the study populations are stated below:

**TABLE 1 – Distribution of cases (Group A) according to Age**

Age Distribution of Cases (Group A)		
Age	Cases (n=50)	Percentage%
20-45 Years	24	48
46-65 Years	25	50
>65 Years	1	2
<b>Total</b>	<b>50</b>	<b>100</b>

Table 1 shows the distribution of cases (Group A) according to age in carcinoma breast.

Minimum age was 23 years and maximum was 73 years. Mean age was found to be  $45.70 \pm 10.929$  years.

Maximum (25) number of cases were found in the age group 46-65 years and minimum (01) number of cases were found in the age group >65 years.

**TABLE 2 – Distribution of Control (Group B) according to Age**

Age Distribution of control (Group B)		
Age	Cases (n=50)	Percentage %
20-45 Years	32	64
46-65 Years	17	34
>65 Years	01	02
<b>Total</b>	<b>50</b>	<b>100</b>

Table 2 shows the distribution of control (Group B) according to age.

Minimum age was 30 years and maximum was 73 years. Mean was found to be  $45.50 \pm 10.053$  years.

Maximum (32) number of cases were found in the age group 20-45 years and minimum (01) number of cases were found in the age group >65 years.

**TABLE- 3 Activity of Alkaline phosphatase in patients with breast cancer (mean  $\pm$  SD, n=50) and control group**

Patient population	ALP (U/L)
Cases	$289.9 \pm 61.3$
Control	$123 \pm 4.7$

Table 3 shows the value of ALP in cases and control group. The mean value was  $289.9 \pm 61.3$  and the mean in control group was  $123 \pm 4.7$  respectively.

### DISCUSSION

The present study was an observational study comprising of 100 patients including 50 cases of carcinoma breast (Group A) and 50 cases as controls (Group B) in Rajendra Institute of Medical Sciences, Ranchi.

Breast cancer is a leading cause of morbidity and mortality in females of developed countries and is the most common malignancy among North American women<sup>[5]</sup>. It is estimated that by the year 2000, 500,000 women worldwide will die from breast cancer. Currently, the most effective way to minimize morbidity and mortality from breast cancer is by early diagnosis and administration of therapy<sup>[6]</sup>.

In our study we found that the mean value of Alkaline phosphatase was  $289.9 \pm 61.3$  and the mean in control group was  $123 \pm 4.7$  respectively which was highly significant ( $p < 0.05$ ).

We found that measurement of plasma total Alkaline phosphatase activity had an overall diagnostic sensitivity and similar to that observed by Coombes et al.<sup>[7]</sup>.

Our studies shows that there is a significantly rise of Alkaline phosphatase which was similar to many small-scale studies suggested that a significant increase in serum ALP was observed in breast cancer patients [8, 9] and it has consistently been shown to predict liver metastases<sup>[10]</sup> and bone metastases<sup>[11,12]</sup>.

## CONCLUSION

Women with breast cancer have ALP activities generally higher than normal healthy women. The progressive increase in the serum ALP activities with breast cancer is an indication of metastasis. The measurement of this parameter may be a useful diagnostic tool in monitoring the disease, its progression and treatment in areas where the facilities for sophisticated studies are not readily available.

## Recommendation

Measurements of Alkaline phosphatase though less sensitive than imaging procedures, can assist in screening and for the early detection and a considerable proportion of metastases and can provide useful objective evidence of their response to treatment.

We recommend serial measurement of Alkaline phosphatase activity for the detection and monitoring of bone metastases, and liver alkaline phosphatase in determination for liver metastases.

## Conflicts Of Interests

No interest to disclose.

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