



SERUM ALKALINE PHOSPHATASE (ALP) ENZYME LEVELS AS A BIOCHEMICAL MARKER IN FEMALES WITH BREAST TUMOR.

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ABSTRACT

Cancer is one of the major causes of mortality worldwide. Carcinoma of breast is the most frequent cancer of women and account for 25% of all cancers. This burden is increasing significantly and in near future it is predicted to be 22 million new cancer cases and 13 million cancer-related deaths occurring annually by 2030. Chronic inflammation is associated with several human cancers and that pro-inflammatory cytokines and other immuno-modulatory molecules can be produced by cells in cancerous tissue to favour tumour growth, infiltration and metastasis. The relationship between chronic inflammation and cancer is complex and bidirectional. This gives idea to take this a comparative study to find out biochemical biomarker in Benign and Malignant breast tumours in females. This study was carried out on total 450 female subjects from Western Rajasthan, age ranging between 21 to 70 years. As tumor progressed with the advancement in growth there was increase in ALP level as noticed in several studies shown to predict bone metastasis and to some lesser extent liver metastasis, as expected on the basis of its biological nature, while some studies have reported fairly sensitivity of ALP for metastases detection, but there are less studies which show its relation with breast cancer so this gives an idea to go for present study.

KEYWORDS : Serum Enzyme Alkaline Phosphates (ALP), Biochemical Marker, Benign, Malignant, Breast, Tumor.

INTRODUCTION

Breast is a dynamic structure, which undergoes changes throughout women's life, and superimposed on these cyclic changes throughout ovarian cycle. The pathogenesis involves disturbance in breast physiology extending from an extreme normal to well-defined disease process.[1]

Cancer is one of the major causes of mortality worldwide. Fairly accurate about 18.1 million new cancer cases and 9.6 million cancer deaths in 2018, as data presented by the International Agency for Research on Cancer (IARC), after focusing on geographic variability across 20 world regions.[2] This burden is increasing significantly and in near future it is predicted to be 22 million new cancer cases and 13 million cancer-related deaths occurring annually by 2030.

The reason for increase in this magnitude of cancer is a consequence of population growth and aging, but with these consequences societal, economic, and lifestyle change are also linked due to increasing human development and are likely to additionally increase the scale and alter cancer trends in the next decades [1].

It is the most frequent cancer of women and account for 25% of all cancers The major types of cancer are carcinoma, sarcoma, melanoma, lymphoma, and leukaemia. The most commonly diagnosed carcinoma originate in the skin, lungs, breasts, pancreas, and other organs and glands. Breast cancer (BC) is the leading cause of cancer death in women. It can be benign and malignant type. Breast cancer is the commonest cancer and leading cause of cancer death in women worldwide, with an estimated 1.7 million cases and over 520,000 deaths in 2012, accounting for 25% of all female cancers and 15% of all female cancer deaths [3].

In various studies ALP activity has shown useful for the diagnosis and clinical evaluation of cancer patients[4]. ALP levels drastically increase in breast cancer patients with bone and liver metastases and are found to be more useful in relapse cases of breast carcinoma^[5].

Women with breast cancer either benign and malignant have higher ALP activities than normal healthy women as number of diseases are related to the elevation of serum ALP level. The increase in ALP level as noticed in several study have consistently been shown to predict bone metastasis and to some lesser extent liver metastasis, as expected on the basis of its biological nature, while some studies have reported fairly sensitivity of ALP for metastases detection.[6] However, the elevation of ALP more than three times of the normal level is generally considered to be specific and sufficient to provide a definite diagnosis of metastasis of breast tumor either in liver and bone.[7]. Although the research conducted on breast cancer is done but studies to show relation Biochemical marker with Benign and Malignant Breast cancer in female in pre-menopause and post menopause are very less in western Rajasthan. So the present study was planned for this mentioned aim.

MATERIAL & METHODS

The present study was conducted in the Department of Biochemistry and Department of Sugary Dr. S. N. Medical College, Jodhpur and Associated Groups of Hospitals. The current study is a case control study and was aimed with primary objective of estimation of **Serum Alkaline Phosphatase (ALP)** Levels in newly diagnosed breast cancer tumor (Benign or Malignant) and to correlate it with the condition of healthy Control.

Study Design: Case Control Study

Sample Size: This study was carried out on total 450 female subjects.

Inclusion Criteria

Females who are willingly participating, aged between 21-70 years., had significant findings of breast lump and with confirmed diagnosed case of breast tumour either benign (neoplastic) or malignant and were going for lumpectomy were included.

Exclusion Criteria

All Females who were not willingly participating , less than 21 years and more than 70 years of age, pregnant and lactating mothers, ongoing menstruation phase of uterine cycle, addicted to smoking, alcohol & tobacco etc, had any history of breast trauma, breast abscess, cystic changes breast diseases and other inflammatory conditions, had any history of breast surgery conducted at least six months, had any history of oral contraceptive drugs at least six months, had any history taking anti-inflammatory drug at least one month, had any history of other chronic diseases presenting with breast lumps, had any history of estrogen and progesterone therapy, particularly that of hormone replacement therapy (HRT treatment for menopausal conditions), and who have any short history of cancer chemotherapy and taking any other cancer treatment like Ayurvedic, Homeopathic etc. and also male were excluded from current study.

Study Groups:

Subjects was categorised into three groups as Healthy, Benign and Malignant, a total:150 subjects were enrolled in each group for this present study.

Group –I: Healthy Control Females (HC: Healthy Control = 150)

One hundred fifty (150) control females aged between 21-70 years having normal vital organ functions and confirmed by routine biochemistry tests were selected from Out Patient Clinics of Hospitals, associated to Dr. S. N. Medical College, Jodhpur.

Group –II: Subjects with Benign Breast Tumour: (BG: Benign Group = 150)

This group included clinically diagnosed cases of hundred and fifty (150) females subjects of Benign Breast Tumour confirmed by histopathological investigations either needle or excision biopsy performed in Clinical laboratories of Department of Pathology.

Group – III: Subjects with Malignant Breast Tumour (MG: Malignant Group = 150)

This group included clinically diagnosed cases of hundred and fifty (150) females subjects of Malignant Breast Tumour confirmed by histopathological investigations either needle or excision biopsy performed in Clinical laboratories of Department of Pathology.

Data Collection:

Female subjects from Western Rajasthan, age ranging between 21 to 70 years and who visited the OPD and enrolled in IPD ward Department of Sugary, for breast tumour surgery either benign or malignant. It was a case control observational study, as an equally number subjects was studied in healthy and breast cancer groups.

A blood sample was taken from antecubital vein with all aseptic conditions. The collected samples were immediately carried to the biochemistry lab and were processed to assess Biochemical marker. The prior ethical permission was taken from the institutional ethical committee and a detailed informed consent form signed wilfully by all the study participants was accepted.

RESULTS:

In present study, the mean ALP values in Healthy control subjects found to be 87.25±19.28 U/L and for benign breast tumor group it was found to be 222.62±73.14 U/L. The difference between the healthy control group and the benign group was found to be significant as shown in table no. 1

Table no. 1. Analysis of Variance of Biochemical Marker: ALP (U/L)

Study Group	Healthy Control	Benign Group	Malignant Group	F value	P value
N = 450	150	150	150		
ALP (U/L) Mean	87.25	222.62	617.34	1087.	0.001
Std. Deviation	19.28	73.14	160.18	81	

Comparing the mean values ALP of benign breast tumor (222.62±73.14 U/L) and malignant breast tumor (617.34±160.18U/L) showed a statistically significant mean difference, $F(2, 447) = 1087.81, p < 0.001$ as shown in table no.1

Table 2. Post Hoc -Tukey HSD Tests of Biochemical Marker: ALP(U/L)

(I) Group	(J) Group	Mean Difference (I-J)	P-tukey
Healthy Control	Benign Group	-135.37	0.001
	Malignant Group	-530.09	0.001
Benign Group	Malignant Group	-394.72	0.001

Further post-hoc Tukey-HSD test revealed that the mean of malignant group is statically higher from every other groups. The mean difference values of serum ALP were significantly increased from healthy control to benign group was -135.37 (95 % CI, 107.60 – 163.14), malignant group to benign group -394.72 (95% CI, 366.95 – 422.49) and malignant group to healthy control -530.09, (95% CI, 502.32 – 557.86), all P_{tukey} values were shown statistically significance mean differences, $P < 0.001$ as shown in table no.2.

DISCUSSION:

In previous studies, ALP activity was shown useful for the diagnosis and clinical evaluation of cancer patients. ALP levels drastically increase in breast cancer patients with bone and liver metastases and are found to be more useful in relapse cases of breast carcinoma., but till date its serum levels in breast tumor patients have been explored in less studies.[8] Several studies shown the role of LDH and GGT in progression of breast tumours has been reported along with ALP levels.[9]

A study conducted by Singh AK et al [10] stratify levels of ALP according to stages of breast malignancy have reported significant increased ALP levels with each stage and found higher level in malignancy with metastatic stage as 809.65 145.97 U/L. Study also presented breast metastasis vs non-metastasis tumours based on cut off values of ALP (/ 500 U/L), reported 61 out of 62 metastases cases had more than 500 U/L ALP levels.

In Indian population, studies conducted by, Prabasheela et al [11], Choudhari A et al [12], Mohammed Saheb et al [13] and Chandrakanth KH et al [14] had reported the mean ALP levels in malignant breast tumor highly significant than control is similar to this study findings between these groups of subjects. The studies conducted by Mishra S et al [15] have reported higher mean value the ALP levels (750.3 102.6 U/L) in malignant breast tumor subjects.

A study conducted by Mohammed Saheb et al [13] Andhra Pradesh population the mean values are similar to the present study (88.88 16.40 U/L). A slightly higher results of mean

(94.85 25.13 U/L) were found by Chandrakanth KH et al[14] in the Karnataka population of India. A previous study conducted by Choudhari A et al[12] in 2013 has reported the mean value 46.49 15.05 U/L in healthy control subjects observed less compared to the present study, whereas in other studies conducted by Mishra S et al[15] and Prabasheela B et al¹¹ (2012), the mean ALP findings (130.0 15.2 U/L and 123.0 4.7 U/L) are higher than the present study. A very few studies were conducted in benign breast tumor group. The mean values of ALP in such study were less (75.48 29.30 U/L) than this study, conducted by Sirivastva V et al[16] in 2016.

Women with breast cancer either benign and malignant shown higher ALP activities than normal healthy women as number of diseases are related to the elevation of serum ALP level. The increase in ALP level as noticed in several study have consistently been shown to predict bone metastasis and to some lesser extent liver metastasis, as expected on the basis of its biological nature, while some studies have reported fairly sensitivity of ALP for metastases detection [6]. However, the elevation of ALP more than three times of the normal level is generally considered to be specific and sufficient to provide a definite diagnosis of metastasis of breast tumor either in liver and bone.[7]

CONCLUSION

Looking at the previous and present study, the management of the female's health whether premenopausal or post-menopausal is the uttermost need of the society. Their regular checkup is very important for their health and management. Thus, it is concluded that estimation of serum ALP being a simple, reliable, economical, and with high sensitivity and specificity should combined with other enzyme markers may be helpful and give more insights for the management of malignant tumor of breast and progression of disease conditions at community-based setups. Further, three to five time elevation of serum ALP activities may provided significant indication of metastasized of breast tumor in liver and bone.

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