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Original Article

Recent Update on Serum Alkaline and Acid Phosphatases in Pre- and Postoperative Breast Cancer Patients

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Abstract

Background: Breast carcinoma in females is an ever-growing malaise with significant mortality and morbidity. In resource-poor settings, the need for a cost-effective and reliable diagnostic tool is of utmost importance.
Methods: In the present study, 54 histopathologically proven breast cancer patients were investigated for their pre- and postoperative serum ALP and ACP levels.
Results: A total of 34 cases (belonging to the age interval of 40–60 years) exhibited a significant drop in serum ALP level after surgery (P = 0.002). Although the serum ACP also showed a postoperative decline, it was not as significant as that of serum ALP.
Conclusion: The role of serum ALP and ACP in the diagnosis, prognosis, and monitoring/surveillance of breast carcinoma cannot be underestimated particularly in third-world countries lacking in medical infrastructure or resource-poor settings.

Keywords: alkaline phosphatase, acid phosphatase, breast cancer, malignancy

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1. Introduction

Alkaline phosphatase (ALP) and acid phosphatase (ACP) are hydrolase enzymes that are active under alkaline and acidic conditions, respectively. They chemically remove the phosphate group from the nucleotides and proteins [1]. Growing children have a comparatively higher levels of serum ALP due to active bone formation and growth. Similarly, males have higher serum ALP level as compared to females, while the difference is neutralized after the age of 60. In females, the serum ALP is elevated during puberty, pregnancy, lactation, and menopause, which is purely physiological [2]. Whereas, ACP is prominently synthesized by the liver, bone marrow, prostate, and

spleen. However, at the same time, the pathological basis of serum ALP elevation also cannot be ruled out, which can be indicative of multi-factorial etiology involving infection of the bone (osteomyelitis), autoimmune disorders (rheumatoid arthritis), CKD (chronic kidney disease), and malignancy [3]. The pathological basis of elevated serum ALP and ACP levels can be associated with infection, inflammation, and infiltration. Serum ALP is the most reliable tumor marker among others like serum ACP, lactose dehydrogenase (LDH), calcium, and serum amyloid-A protein (SAA) in breast carcinoma [4]. Serum ALP estimation is a cost-effective and reliable diagnostic tool in breast cancer, particularly in third-world countries that lack the infrastructure for the modern-day diagnosis of breast cancer [4]. The serum ALP level is known to rise proportionally with the advancing stage in breast cancer [5]. Breast carcinoma, like other types of malignancies, is a cumulative outcome of multiple predisposing factors which interactively initiate carcinogenesis. The prevalence of breast carcinoma increases with advancing age, particularly post-menopausal females are more prone to malignancy. Cessation of a menstrual cycle is followed by altered biochemistry of female sex hormones and hence increased risk of breast carcinoma [6]. The clinical presentation of breast cancer includes multiple symptoms, which are often ignored by patients leading to the delay in medical intervention which resulted in mortality and morbidity related to the disease [7]. In the absence of metastatic spread, the surgical resection of the tumor can normalize the elevated serum ALP level in breast cancer patients, thereby indicating a good prognosis [8].

There are numerous missing links in the studies regarding variation in the level of serum ALP and ACP in breast carcinoma. The underlying cause of elevated ALP and ACP levels needs to be investigated thoroughly to diagnose the malignancy in its early stage. The real-time use of serum ALP and ACP as a diagnostic and prognostic tool is possible only if the knowledge gaps and missing links are well understood and worked upon. Therefore, the present study investigates the role of serum ALP and ACP pre and post operative surgery in breast cancer patients.

2. Materials And Methods

All protocols, procedures, and instrumentation were standardized according to the setting in the Department of Medical Laboratory Sciences, Khalsa College of Pharmacy and Technology, Amritsar.

2.1. Permission

The study was approved by the Doctoral Advisory Committee, Institutional Research Committee, and Institutional Ethics Committee of Adesh University, Bathinda. Permission was granted by the competent authority of Government Medical College and Hospital (GMC&H), Amritsar for the collection of blood samples of breast cancer patients from July 2017 to July 2018.

The inclusion criteria for this study were: female patients with histopathologically proven malignancy breast cancer, patients with diverse demography (rural/urban) and socioeconomic status, nonpregnant female subjects, patients without autoimmune disorders (rheumatoid arthritis) and bone infections (osteomyelitis), aged >20 years, having no liver disease (cirrhosis), chronic kidney disease and hemodialysis, and mentally fit to provide informed consent and relevant information related to the disease.

2.2. Sample collection

Fasting 2 ml of blood was drawn by venipuncture under aseptic conditions before and after the surgery (pre and postoperatively) after written informed consent was obtained from the breast cancer patients. The needles and syringes were discarded according to the protocol for biomedical waste management.

2.3. Transportation

Blood samples were immediately transported (with 4°C temperature maintained in a cool box) to the clinical laboratory for further processing.

2.4. Enzyme assay

Blood samples were centrifuged at 2500 rpm for 15 min to obtain serum. P-Nitrophenyl phosphate kits for serum ALP and serum ACP were used to measure serum ALP and ACP on a semi-automated analyzer (Erba Chem 5 Plus V2). Absorbance readings were taken at 405 nm wavelength with temperature maintained at 37°C. The manufacturer's guidelines were followed throughout the procedure. Readings were reported in IU/L.

2.5. Statistical analysis

All necessary analysis was done using MS-Excel 2007. The means or frequencies of patient demographics were interpreted. The variation between pre and postoperative values of both serum ALP and ACP was analyzed by using unpaired *t*-test. *P*-value ≤ 0.05 was considered statistically significant.

3. Results and Discussion

The present study reported 54 breast cancer patients registered at Government Medical College and Hospital (GMC&H), Amritsar. According to the age interval, the participants were divided into different age groups (Table 1). Among them, the most affected age group was 40–49 years (37%) followed by 50–59 years (26%). Similar results were reported by the American Cancer Society, Indian Cancer Society, and NCBI. Whereas, Anders et al [9] reported the incidence of early onset of breast cancer in females. In the current study, early onset of malignancy (12.96%) related to the age interval of 30–39 years had been reported. Data reported by NCBI and NIH (2019) reveals that 11% of breast cancer cases occur in women <40 years of age. The early onset of breast carcinoma among young females is alarming and ever-increasing. Predisposing risk factors are prolonged use of oral contraceptives, high animal fat intake, and low BMI in premenopausal females [10], whereas non-modifiable risk factors include familial predisposition and gene mutations [11]. In the present study, familial predisposition cases (7.4%) belonged to the age interval of 50–59 years (Table 1). Rural and urban distribution of patients in the current study was found to be 64.82% and 35.18%, respectively. According to the World Bank collection of development indicators (2018), 65.97% of the Indian population resides in the rural belt. Also, it is the rural population which owing to their low socioeconomic status visits exclusively government hospitals for treatment. In total, 54 cases were confirmed for the malignancy (malignant breast lesions) as supported by FNAC findings. Of them, 19 subjects were confirmed with stage II, whereas the remaining 35 had stage-III presentation. Furthermore, all of the stage-III patients were identified with axillary lymphadenopathy (Table 2).

Out of the 54 confirmed malignant cases, 44 had a painless lump (81.48%), while 10 had a painful lump (18.51%). A painless lump is a more common clinical feature among breast carcinoma patients [12]. Further, in the current study, ulceration of skin over the lump (18.51%) was also reported. Breast cancer with skin ulceration is considered a locally advanced disease [13]. The finding of skin ulceration as a symptom of locally advanced

Table 1: Demographics of breast carcinoma patients.

Age interval (yr)	N = 54	Percentage
30–39	07	12.96%
40–49	20	37.03%
50–59	14	25.92%
60–69	07	12.96%
70–79	06	11.11%
Rural	35	64.82 %
Urban	19	35.18%
Familial predisposition	04	7.40%

Table 2: Distribution of breast cancer patients according to their symptoms.

Clinical symptoms		No. of patients	Percentage
Stage (TNM)	II	19	35.18%
	III	35	64.81%
Axillary Lymphadenopathy		35	64.81%
Lump	Painless	44	81.48%
	Painful	10	18.51%
Ulceration of skin over lump		10	18.51%
Skin changes (skin texture changes) of the breast involved		09	16.66%
Nipple discharge		08	14.81%
Weight loss		05	09.25%
Anorexia		07	12.96%
Malignant lesions		54	90.0%
Benign lesions		06	10.0%
Malignant + benign lesions		60	100%

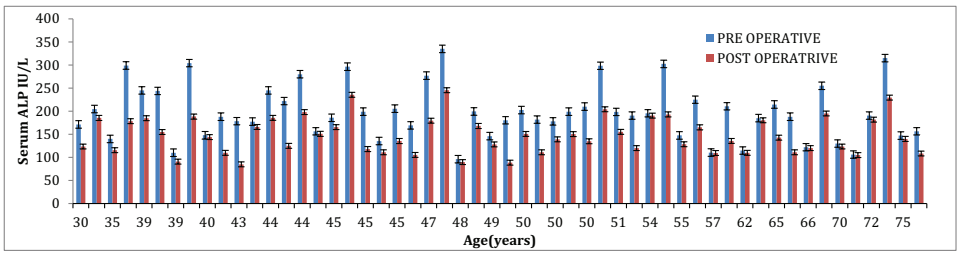

Figure 1: Pre- and postoperative serum alkaline phosphatase levels in different age groups of breast carcinoma.

breast carcinoma and inflammatory breast cancer is a deciding factor for early diagnosis and the choice of treatment and its outcome. The breast skin changes were observed in 16.66% of cases whereas 14.81% of patients reported nipple discharge after skin changes in the breast. As reported earlier, nipple discharge is a characteristic feature of ductal carcinoma in situ ranging from 2% to 13% in clinical presentation [14]. The typical symptoms of breast carcinoma like a lump, ulceration, and pigmentation of skin over

Table 3: Comparison of pre and postoperative levels of serum ALP and ACP in different age groups of breast carcinoma.

Breast carcinoma		ALP IU/L			ACP IU/L		
Age (yr)		No. of cases	Mean ± SD	P-value	No. of cases	Mean ± SD	P-value
30–39	Preoperative	07	202.02 ± 66.16	0.0841	07	0.70 ± 0.07	0.1064
	Postoperative		147.71 ± 37.97			0.62 ± 0.07	
40–49	Preoperative	20	207.24 ± 63.61	0.0029	20	0.72 ± 0.13	0.0812
	Postoperative		151.79 ± 44.98			0.65 ± 0.11	
50–59	Preoperative	14	201.46 ± 50.36	0.002	14	0.72 ±0.11	0.2249
	Postoperative		145.81 ± 34.02			0.67 ± 0.10	
60–69	Preoperative	07	184.32 ± 50.57	0.091	07	0.76 ± 0.32	0.620
	Postoperative		142.17 ± 33.61			0.69 ± 0.21	
70–79	Preoperative	06	174.22 ± 74.46	0.4868	06	0.66 ± 0.12	0.6577
	Postoperative		148.0 ± 48.72			0.62 ± 0.12	

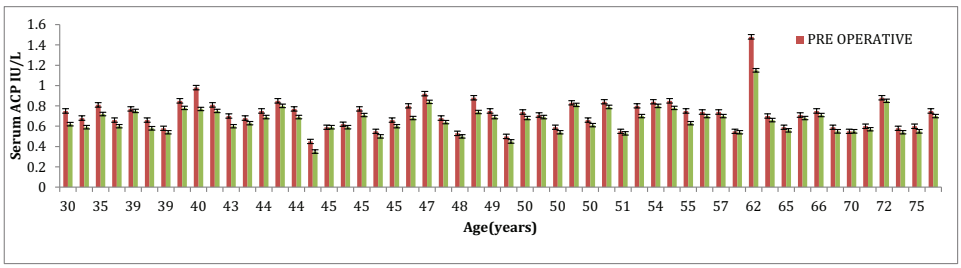

Figure 2: Pre- and postoperative serum acid phosphatase levels in different age groups of breast carcinoma.

the lump, nipple discharge, and lymphadenopathy (axillary or generalized) have been reported in many studies related to breast cancer with minor variation in their distribution (NCBI, American Cancer Society). Henceforth, weight loss in breast carcinoma can be attributed to the stage of cancer, (as the stage advances, the nutritional demand of cancer cells increases as is the cancer load) and the psychological stress related to malignancy and anorexia. Therefore, the current study reported five cases with significant weight loss (>10% of body weight) accounting for 9.25% of breast cancer patients (Table 2). In addition, loss of appetite (anorexia) was reported in seven patients (12.96%). Both weight loss and anorexia resulted to be the outcome of psychological

stress related to cancer, altered biochemistry, the nutritional burden of caner load, and diminished taste and smell perceptions [15].

Comparison of pre and postoperative levels of serum ALP and ACP was undertaken statistically to find any significant variation. The age group 40–49 years (n = 20) exhibited a statistically significant drop (postoperatively) in the level of serum ALP from 207.24 ± 63.61 to 151.79 ± 44.98 (p = 0.002) (Table 3, Figure **1**). However, the drop for serum ACP was from 0.729 ± 0.137 to 0.657 ± 0.117 (Table 3, Figure **2**). The age group 50–59 years (n = 14) also exhibited a statistically significant difference (p = 0.002) for the decline in postoperative serum ALP level from 201.46 ± 50.36 to 145.81 ± 34.02, thus reinforcing the use of serum ALP as a cost-effective tumor marker in breast carcinoma in poor resource settings [16].

Serum ACP levels in pre and postoperative cases in age groups 40–49 and 50–59 years showed a statistically insignificant drop from 0.72 to 0.65–0.67 IU/l with p-values 0.081 and 0.224, respectively (Table 3). The maximum number of patients (20 + 14 = 34) showing a significant drop in serum ALP levels postoperatively belonged to the age group 40–60 years, which had the largest number of cases. Similarly, a significant drop in serum ALP postoperatively in all stages has been reported earlier [8].

4. Conclusion

The most common symptom of breast cancer is a lump or mass in the breast, which in most cases is painless. Other findings are axillary lymphadenopathy, nipple discharge, ulceration of skin over the lump, and changes in the skin texture of the breast involved. The role of serum ALP and ACP as tumor markers has its advantages in resource-poor settings. Furthermore, the high prevalence of breast carcinoma among females of developing countries reinforces the use of serum ALP and ACP as cancer markers in resource-poor settings. Therefore, studies will be required to establish the value of serum ALP to predict the prognosis, diagnosis, and monitoring of breast cancer.

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Nil.

Ethical Considerations

The current study was approved by the institutional ethics committee of the Government Medical College, Amritsar (Code no. GMCIEC00104).

Competing Interests

There are no conflicts of interest.

Availability of Data and Material

All relevant data of this study are available to any interested researchers upon reasonable request to the corresponding author.

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