



Research Article

Serum Albumin Levels in Breast Cancer: Correlation with Overall Survival

Raman Preet Kaur¹, Rubal², Monisha Dhiman², Rajesh Vashittha³ and Anjana Munshi^{1*}

Abstract

Introduction: Albumin is an important biomarker that indicates malnutrition as well as inflammation. The aim of the study was to evaluate the albumin levels in breast cancer patients and its association with overall survival among breast cancer patients of Malwa region of Punjab.

Material and methods: The study was planned in Malwa region of Punjab. Sampling was done from Guru Gobind Singh Medical College and Hospital and Max Hospital. The estimation of albumin levels was done at Central University of Punjab. 250 patients with breast cancer and 250 age and sex matched controls were involved in the study. Albumin levels were estimated using fully automated bio analyzer Erba 200. Follow-up interviews were conducted at an interval of 3, 6, 12 and 15 months to determine the outcome among breast cancer patients.

Results: Low levels of albumin was found among the diseased in comparison with controls ($p < 0.000$). Higher albumin levels associated significantly with overall survival in breast cancer patients [χ^2 : 11.95, $p < 0.000$; odds ratio: 7.636 (95% CI, 2.047-28.49)].

Conclusion: Elevated levels of albumin (>3.5 g/dl) are associated significantly with increased overall survival among breast cancer patients. Albumin estimation may be a simple and inexpensive tool for the risk assessment and outcome of the disease in Malwa region of Punjab where the incidence of breast cancer is reported to be very high.

Keywords

Breast cancer; Albumin; Survival; Malnutrition

Introduction

Breast cancer represents nearly quarter (23%) of all the cancers [1]. Million and a half new cases of breast cancer are reported every year [2]. The estimated number of breast cancer patients in the US was reported to be 2,31,840 in 2015 [3]. The global burden is expected to cross 2 million by the year 2030. In India, breast cancer is the most common cancer with a relative proportion ranging from 19.3%-27.5% (ICMR). According to the Department of Health and Family Welfare, the cancer graph of Punjab, a northern state in India is rising

abruptly. Malwa region of Punjab has come under focus on account of its increasing cancer incidence (1089/million/year) in comparison with another region, Majha (647/million/year) and Doaba (881/million/year) [4].

The key factors determining cancer survival include genomic alterations, age, stage, number of metastatic sites, the location of metastasis, quality of life and malnutrition [5,6]. Malnutrition is one of the most significant problems in cancer patients due to different mechanisms involving tumor, host response to tumor and anticancer therapies [7]. Malnutrition has been correlated with different clinical consequences like deteriorated quality of life, decreased response to treatment, induced toxicity due to chemotherapy and reduction in cancer survival [8].

Philips et al. [9] carried out a pioneer study that showed an inverse relationship between albumin levels and many adult onset disorders including cancer. In our previous study we have identified that serum albumin levels associated significantly with poor outcome among ischemic stroke patients [10]. Serum albumin levels are usually assessed to detect the malnutrition and inflammation status among the cancer patients because malnutrition, as well as inflammation, has been reported to inhibit the albumin synthesis. In adults the normal albumin range is 3.5-5.0g/dl; less than 3.5 g/dl is called hypoalbuminemia [11-12]. During initial stages of breast cancer, enhanced albumin synthesis is detected in metabolically affected patients but during later stages of the disease, inflammation and malnutrition inhibit albumin synthesis [13]. So serum albumin levels are usually assessed to evaluate the nutritional status of patients, disease progression and as a prognostic marker [5]. Therefore, the aim of the present study was to assess the albumin levels in breast cancer patients from Malwa region of Punjab State where breast cancer is widely feared and also to determine the relationship between albumin levels with overall survival.

Material and Methods

Two hundred and fifty breast cancer patients (Females: Males=244:6) were evaluated at Guru Gobind Singh Medical College & Hospital, Faridkot and MAX hospital, Bathinda, Punjab. The study was approved by ethical committee of the Central University of Punjab as well as study hospital. All the patients were examined by an oncologist and mode of diagnosis included fine needle aspiration cytology (FNAC), mammography and histopathology. All patients underwent FNAC. Patients with major cardiac, renal, hepatic, skeletal disorders and neurological disorders were excluded from the study. The control group included 250 healthy individuals, with no disease history, belonged to the same ethnic group and matched for sex and age. Information about the demographic profile and risk factors was collected by using a structured questionnaire.

Blood samples and albumin estimation

Blood samples for assessment of albumin levels were collected from patients. Blood samples were subjected to centrifugation immediately after collection and stored at -80°C until analysis. The levels of albumin were estimated in g/dl. Albumin analysis was performed by using a commercially available kit procured from ERBA

*Corresponding author: Anjana Munshi, Professor and COC, Centre for Human Genetics and Molecular Medicine, Central University of Punjab, Bathinda, India, Tel: +919872694373; E-mail: anjanadurani@yahoo.co.in

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Mannheim. The principle of the assay is that albumin binds with Bromo Cresol Green (BCG) at pH 4.2 causing a shift in absorbance of yellow BCG dye. The blue-green color formed is proportional to the concentration of albumin, when measured photo metrically between 580-630 nm with maximum absorbance at 625 nm. The standard reference value of albumin ranges from 3.5 g/dl-5.2 g/dl.

Follow-up

The follow-up of the patients was conducted personally during their follow-up visits to the hospital or telephonically at an interval of 3, 6, 12 and 15 months after hospital discharge. Follow-ups were carried out to check the overall survival, metastasis, recurrence and death.

Statistical analysis

The data was expressed as mean ± SD. The data was not standard. It was positively skewed, so non- parametric Mann-Whitney U-test was performed for comparison of mean values of albumin among cases and controls. The association of albumin levels with outcome including death, recurrence and metastasis was estimated by odds ratio with 95% confidence interval (CI) and χ^2 analysis using Open Epi software (Open Epi version 2.3.1 from Department of Epidemiology, Rollins school of public health, Emory University, Atlanta, GA 30322, USA).

Results

250 patients along with 250 healthy controls were included in the study. All the cases, as well as controls, were from Malwa region of Punjab where the primary ethnic group is Jatt Sikhs. The mean age of the patients at the time of disease presentation was 53.62 ± 12.31 years. 55% of patients were from the urban area. None of the patients were pregnant at the time of disease. 7.2% of the patients were underweight and 55% were obese. The family history of cancer including breast and other cancers was observed in 12% of the study group (Table 1). 48% of patients had exposure to pesticides since these the patients belonged to the farming community.

55% of patients suffered from left breast carcinoma. Modified radical mastectomy (MRM) was performed in 63% of population along with lumpectomy in 5% of the patients. All the patients underwent chemotherapy. Prevalent histological subtype was infiltrating ductal carcinoma followed by infiltrating lobular carcinoma, *in situ* lobular and ductal carcinoma. ER/PR and HER-2 status was available for 93 and 81 patients respectively. Among these 62.3% and 49.3% patients were negative for ER/PR and HER2 respectively. 17.5% of the patients were suffering from triple negative breast cancer, which is the most aggressive type of breast cancer (Table 2).

The levels of albumin were significantly decreased in the patients in comparison with controls (Table 3) and showed a significant association with the disease (p<0.000). As per follow-up interviews, death was reported in 26% of the diseased population followed by metastasis and recurrence in 21% of population. However, high albumin levels (>3.5g/ml) showed significant association with overall survival in breast cancer patients (χ^2 : 11.95, p<0.000; odds ratio: 7.636 (95% CI, 2.047-28.49).

Discussion

This study is one of its types in Malwa region of Punjab, where cancer is widely feared. Albumin is a readily detectable marker that can be used to assess nutritional status, the severity of disease, disease

Table 1: Demographic profile of patients.

Personal data	Item	Number	%
Gender	Male	6	2.4
	Female	244	97.6
Marital Status	Married	249	99.6
	Unmarried	1	0.4
Menopausal Status	Premenopausal	85	34.84
	Postmenopausal	155	63.52
	Hysterectomy	4	2.04
Parity	Parent	246	98.4
	Nulliparous	4	1.6
BMI	Obese	112	45
	Normal	120	48
	Underweight	18	7
Pregnancy at presentation	Yes	0	0
	No	244	100
Family history	Breast cancer	11	4.5
	Other	19	7.5
Pesticide exposure		120	48

Table 2: Tumor biomarker characteristics and treatment strategies.

Receptor	Status	Number	%
ER (n=93)	Positive	35	37.6
	Negative	58	62.3
PR (n=93)	Positive	35	37.6
	Negative	58	62.3
HER-2 (n=81)	Positive	41	50.6
	Negative	40	49.3
Subtype (n=80)	Triple negative	14	17.5
Surgery	MRM	126	63
	Lumpectomy	10	5
Chemotherapy	Yes	200	100
	No	0	0

ER: Estrogen receptor, PR: Progesterone receptor, MRM: Modified radical mastectomy

Table 3: Overall Albumin levels in breast cancer patients as well as controls.

Group (n)	Albumin levels	P value
Patients (250)	4.003018868 ± 0.657521801	<0.001
Controls (250)	4.522559524 ± 0.473909712	

progression and prognosis. In the present study, we have found that albumin levels in breast cancer patients were significantly low in comparison with healthy controls. It has been found that there is an inverse correlation between body weight index and albumin synthesis in initial cancer stages in metabolically affected patients but during advanced cancer stages malnutrition and inflammation suppress albumin synthesis in breast cancer patients [14]. Ballmer et al. [14] also found that in later stages of cancer albumin synthesis is suppressed. Two French studies have reported malnutrition in breast cancer patients to be 20.5% [15] and 18.3% [16]. Several studies in different populations have demonstrated that increased serum albumin levels in breast cancer patients is a strong predictor of functional outcome. In the present study, we observed a significant association of high albumin levels (>3.5 g/dl) with overall survival as reported in earlier studies. Liu et al. [17] found that patients with higher albumin levels had 45% reduced the risk of death in comparison with patients with lower albumin levels. It has been reported that

higher albumin levels increase cancer patient survival by 72%. Several studies have demonstrated that albumin levels may be associated with poor prognosis of different types of solid cancers including lung cancer, breast cancer, gastrointestinal cancer and ovarian cancer [5,18]. Lis et al. [19] carried out a retrospective study to check the effect of baseline serum albumin levels in 180 breast cancer patients and found that low albumin levels are related with poor survival ($p=0.0033$). Heys et al. [20] reported serum albumin, lymph node involvement and advanced cancer stage to be independent prognostic markers. According to Wyld et al. [21] albumin levels, advanced age and estrogen receptor negativity are related with reduced overall and disease-free survival in breast cancer patients with hepatic metastasis. Liu et al. [17] conducted a study including 2425 Caucasian patients and found reduced albumin levels to be associated with reduced disease-free survival, overall survival, disease and recurrence. Among cancer patients, serum biomarkers are promising clinical prognostic factors, but a single biomarker might not have sufficient predictive power for clinical application. So a combination of different markers should be used.

In conclusion, the present study indicates that the elevated levels of albumin are associated with increased survival rate. Increased risk of mortality was observed in patients with reduced levels of albumin. So, Albumin estimation can be used as a marker for the risk assessment of disease in the Malwa region of Punjab, where the incidence of breast cancer is high.

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Compliance with Ethical Standards

The blood sample collection of breast cancer patients for the present study was approved by Institutional Ethics Committee (IES) of CUPB.

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Author Affiliation

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¹Centre for Human Genetics and Molecular Medicine, Central University of Punjab Bathinda, Punjab, India

²Centre for Biochemistry and Microbial Sciences, Central University of Punjab Bathinda, Punjab, India

³Max Hospital, Bathinda, India

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