



**ORIGINAL RESEARCH PAPER**

**General Surgery**

**SERUM LDH AS PROGNOSTIC MARKER IN BREAST CARCINOMA PATIENTS**

**KEY WORDS:** LDH, carcinoma breast, prognosis, staging

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**ABSTRACT**

Breast cancer is the second leading cause of cancer related deaths in women and is the most common cancer in females, accounting for 23% of all cancer cases. So, early detection of carcinoma is necessary. For early detection of carcinoma, a number of biochemical markers have been studied to evaluate the malignancy-ferritin, gamma glutamyl transferase, carcino-embryonic antigen, sodium dismutase, alkaline phosphatase, glutathione, cholinesterase-but, none of them are ideal and are very expensive for regular follow up. LDH is the simplest and cheapest to measure. LDH is a 140kDa tetramer molecule that exists in 5 major iso-enzymes, numbered LDH1-LDH5. These iso-enzymes are formed by the association of 2 different types of 35kDa subunits-M (muscle) and H (heart), encoded by LDH-A and LDH-B genes respectively. A rapid increase in the number of malignant cells, modulates the LDH level in cytoplasmic compartments of cells, due to upregulation in its gene. This increased LDH level is helpful for fulfillment of metabolic requirement and anaerobic glycolysis in these malignant cells. The value of LDH was found to be specific in patients with breast malignancy and also corresponds with TNM staging. Here, in this study an attempt has been made to check serum LDH as a marker for prognosis of breast cancer.

**1. Introduction**

Breast cancer is a heterogenous disease. About 6% of all breast tumours present with distant metastasis at diagnosis. Worldwide breast cancer is the most common cancer in females with age-adjusted incidence rates of 124/1,00,000 population in USA. The incidence of breast cancer is less in India as compared to western world, however it is rising cancer of urban Indian women and the second to carcinoma cervix in the rural women. The age-adjusted incidence rates (AARs) ranges from 6.2 to 39.5 per 1,00,000 Indian women, one third that of Western countries with disproportionately higher mortality rate. While cancer account for high morbidity and high mortality rate throughout the world, cancer of breast is common in women in developed countries and more than 40% of all breast cancer cases are found in developing countries. Owing to the lack of awareness of this disease and in absence of breast cancer screening program, the majority of breast cancers are diagnosed at a relatively advanced age. The recent emphasis on health education, early diagnosis of cancers, and more public facilities for cancer treatment are expected to bring about the much needed improvement in breast cancer care in India. Cancer that is detected early can potentially be cured when the tumour is small enough to be completely removed surgically. Unfortunately, most cancers do not produce any symptoms until the tumours are either too large to be removed surgically or cancerous cells have already spread to other tissues, ie, metastasis has taken place. LDH is the most important metabolic enzyme involved in glycolysis, as it can convert pyruvate to lactate at the end of glycolysis and was found to be specific in patients with breast malignancy. Hence, in this study, we will be correlating the values of LDH in patients with carcinoma breast and see whether LDH can be used as a prognostic marker in these patients.

**2. Materials and method**

**Study:** The study included 30 females age matched controls who do not have any other breast diseases and 30 females study subjects who had pathologically proven **BREAST CANCER**.

**Study design :**

- 1) Serum LDH values were estimated in study and control group.
- 2) Pre intervention
- 3) Post intervention

**Study population:**

After seeking informed consent all the patient with breast cancer and controls who were willing to adhere to the estimation of serum LDH pre and post intervention i.e. Surgery / chemotherapy.

**3. Results**

In my study, total 60 patients were taken. Now , these patients were divided into 2 groups.

Group 1: 30 patients: Study group: Females with pathologically proven breast cancer

Group 2: 30 patients :Control group: Females with no breast disease.

In the first table, the levels of serum LDH is compared.

**TABLE 1**

LDH before intervention	Group 1	Group 2	Total	p-value
Normal (230-460)	15	27	42	0.002
Abnormal (> 460IU/l)	15	3	18	
Total	30	30	60	

Out of 30 patients in study group, 15 patients had increase in serum LDH level. By using Fisher's exact test p-value is 0.002. So, serum LDH was found to be significantly raised in patients with carcinoma breast.

Now, intervention was done in 15 patients of the study group, with increased serum LDH level.

7 patients underwent chemotherapy and 8 patients underwent surgery.

**TABLE-2**

Intervention	Abnormal LDH in patients after intervention	Decreased LDH levels in patients after intervention	Total number of patients
After chemotherapy	1	6	7
After surgery (POD-7)	6	2	8
Total	7	8	15

Out of 7 patients, who underwent chemotherapy, 6 patients had decrease in the level of serum LDH after chemotherapy. 8 patients underwent surgery and serum LDH was measured in POD-4. It was seen that LDH was decreased only in 2 patients.

Now, the study population was divided into 2 groups according to the age group.

**TABLE-3**

Age group	Group 1	Group 2	Total	p-value
<30	0	5	5	
31-40	5	7	12	
41-50	10	8	18	
51-60	6	6	12	0.175
61-70	7	3	10	
>70	2	1	3	
Total	30	30	60	

By using Fisher's exact test p-value > 0.05 therefore there is no significant difference between age distribution in group 1 and group 2.

**TABLE-4**

Group	Number of patients	Mean (age in years)	Standard deviation (age in years)
Group 1	30	53.47	11.53
Group 2	30	45.27	13.81

  

Age group	Mean LDH in group 1	Mean LDH in group 2
<30	00	279.5
31-40	601	288.57
41-50	433.22	322
51-60	494.16	378.16
61-70	585.71	293.66
>70	470	287

LDH is increased in the age group 31-40yrs in the study population. LDH is increased in patients >50yrs in the study population. LDH is within normal level in the control group.

In table-5, mean LDH is observed in different stages of breast carcinoma.

**TABLE-5**

Stage	No of pts	Mean LDH
I	0	0
II	19	448
III	10	823.66
IV	1	800

It is seen that LDH is significantly raised in stage III and stage IV breast carcinoma (late onset breast carcinoma).

**4. Discussion**

Breast cancer is the most common cancer among women and the second leading cause of cancer related death. About 6% of all breast tumours present with distant metastasis at diagnosis.

LDH is a ubiquitous enzyme that plays a central role in anaerobic glycolysis, as it catalyzes reversible conversion of pyruvate into lactate. LDH comprises a family of 6 tetrameric isoenzymes, with a tissue specific expression regulated by both physiological and pathological conditions. The LDHA gene expression is upregulated in several types of cancers, especially in rapid growing tumours, to maintain glycolysis as an alternative source of energy during hypoxic stress and subsequent high LDH level in cytoplasmic compartment.

Different extra-cellular factors, such as hormones, growth factors, and cytokines can regulate LDH expression by receptor-dependent and independent intracellular signaling pathways.

LDH is a well known marker of tissue damage. Many pathological conditions, including cancer, present with LDH elevation due to acute cell death or necrosis. Moreover, high plasmatic LDH levels influence tumour progression and metastatic spread with a negative impact on outcome in various cancer types.

The first piece of evidence dates back to the late 1990s and 2000s when three extensive studies found that elevated plasmatic LDH levels were associated with poor outcome in metastatic breast cancer patients. High plasmatic LDH levels were also proven to be associated with increased risk of disease recurrence and death. Notably, a recent meta-analysis confirmed these findings in both metastatic breast cancer and early breast cancer.

In a study, previously, it was found that on post-operative day - 7, serum LDH levels were significantly raised. But, subsequently, there was decline in LDH levels, post-operatively at 1 month, 3 months and 6 months, proportional to the therapeutic response. This increase in serum LDH levels, in the first week, following surgery, suggests radical destruction of cancer cells resulting in the release of enzymes into the circulating system and could be initiated by the tumour itself in a bid to survive the hypoxia induced by destruction of tumour vasculature and tissues, the underlying principle behind all anti-cancer treatment.

Persistent rise of serum LDH levels is because of poor response to treatment or metastasis or recurrence.

In an explorative analysis of prognostic value of LDH for survival in patients with triple negative breast cancer, it has been found that serum LDH levels were significantly associated with younger age of cancer onset and poor prognosis. Greater metastatic sites reflect heavier tumour burden and younger patients tend to have poor prognosis as compared to older patients.

**5. Conclusion :**

The prognostic value of serum LDH for survival in patients in breast cancer patients has been investigated in several studies. However, it is still difficult to confirm the prognostic role of serum LDH in breast cancer. In my study, the sample size was small and long term follow up could not be done. Therefore, meta-analysis with a large sample size and follow up will be beneficial.

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