



# **Study of Clinical Profile of Carcinoma Breast and Prognostic Significance of Serum Lactate Dehydrogenase as Tumor Marker in Carcinoma Breast**

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## **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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**Study Protocol**

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## **ABSTRACT**

**Background:** Breast cancer is the highly prevalent malignancy and is a major killer in women around world. In India, there is substantial statistically significant increase in breast cancer incidence patterns. Women from under developed areas(883000 cases) have a significantly higher no. of cases than those from developed areas (794,000) [1]. There are various risk factors associated with breast malignancy. A variety of bio-chemical markers have been tested to determine the malignancy, for the early detection of carcinoma of different origin. LDH is the easiest and cheapest to calculate of all of these indicators.

### **Objectives:**

- To study the clinical profile of patient with breast cancer.
- To study the prognostic significance of LDH as tumor marker in breast cancer.
- To compare post-operative LDH level in patient undergoing surgery for carcinoma breast v/s patient undergoing neoadjuvant chemotherapy.

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> Compare variation in preoperative baselines LDH levels and post-operative LDH levels.  
**Methodology:** It is a prospective observational study done on patients with breast cancer. It will be conducted at Dept. of General Surgery , J.N.M.C and AVBRH, Sawangi (Meghe), Wardha. The study will be conducted on patients with Carcinoma Breast.  
**Results:** To be assessed after the study.  
**Conclusion:** Serum LDH is a good prognostic marker of breast cancer.

*Keywords: Breast cancer; LDH.*

## 1. INTRODUCTION

Breast cancer is the highly prevalent malignancy and leading cause of death among woman around the world. In India, there is substantial statistically significant increase in breast cancer incidence patterns. During the last two decades, the mortality rates associated with breast cancer also increased. The annual age-standardized rate for BC incidence in India is 25.8/100,000, with a high mortality rate of 12.7/100,000. Breast cancer is clinically, genetically and biochemically heterogeneous. In Asian countries the Prevalence rate of breast carcinoma is significantly less than in western countries. The incidence of Breast cancer is rising, with the majority of the increase seen in developed countries. India's age-standardized breast cancer incidence rate is one-third that of Western countries. Breast Cancer is the commonest female malignancy world-wide, accounting for almost one fourth of all cancers with an estimated 1.6 Million new cases of cancer diagnosed in 2012. Women from lower developed countries (883, 000 cases) have a significantly higher no. of cases than those from developed countries (794,000) [1,2].

Risk factors that modulate breast cancer development addressed in this analysis include: age, geographical area and socio-economic status, obstetrics history , exo-genous hormones, risk factors in lifestyle( Alcohol, diet, obesity and physical activity), family H/O breast carcinoma, mammography Density, H/O benign breast disease, ionizing-radiation, bone density [3].

Breast cancer is a heterogenous pathology and has varying clinical properties. T.N.M. staging method is nowadays commonly used for prognosis of cancer. However, after chemotherapy the survival among Breast cancer patients differs significantly, often in the same stages. Several clinico-pathological variables, such as patient age, status of menopause, size of the tumor , level of LN, grade of tumour,

receptor of estrogen, receptor of progesterone, EGF receptor(HER-2) with expression of Ki67 parameters have been established to the formulation of the treatment plan. More and more serum bio-markers have recently been thought of, Prognostic factors for breast cancers include circulating micro-RNAs, inflammatory factors and stem cells markers 4 and 6.

Such reliable markers may provide new insights in patient with breast cancer [4,5]. In most cases (94.1 percent) FNAC was performed for breast cancer diagnosis and a positive predictive value of 85.3 percent was obtained. FNAC is a valuable tool for diagnosis, since it is quick and cost efficient. The use of mammographic or ultrasonographic guidance for biopsy with core needle (CNB) and biopsy with vacuum assistance is increasingly being used for non-palpable tumours. Unfortunately, in this part of the world these strategies haven't been picked up, perhaps because of their inherent expense. Mammography is an effective method for screening breast carcinoma between 50 and 70 years, as the volume of the breast tissue decreases and the fat content increases.

Highest incidence involving breast cancer is seen in fifth decade in studies from India, including our research. During this age, the breast tissue content is high and therefore mammography's effectiveness in detecting breast cancer during screening is likely to be reduced.

A variety of bio-chemical markers have been tested to determine the malignancy for detecting different origins of Breast cancer. Serum biochemical markers of Ferritin, Gamma-Glutamyl-Transpeptidase (GGT), Carcinoembryonic-Antigen (CEA), Superoxide Dismutase(SOD), Alkaline-Phosphatase(ALP), glutathione, phospho-hexose isomerase, leucine aminopeptidase and Cholinesterase are used for breast malignancy. LDH is the easiest and cheapest to calculate of all these indicators. LDH is released from cells in response to cell

damage, causing its baseline level to rise in the extracellular space and the bloodstream or other body fluids. Therefore, LDH has been recommended as a general marker of cell/tissue injury or to help identify the type of cells or tissues that are damaged. Various testing methods are applied to measure LDH, both quantitatively and qualitatively, either as a total protein or as an individual LDH isoenzyme. It requires serum LDH enzyme for anaerobic glycolysis of these malignant cells. Rapid rise in malignant cells modulates LDH levels in cellular cytoplasmic-compartment due to upregulation in its genes. This causes raised serum LDH level in Breast cancer patients. Which is helpful in fulfilment of metabolic requirements as well as anaerobic glycolysis of malignant cells. The serum LDH values found to be variable in breast malignant patients which correlates with TNM staging [1]. Elevation in plasma LDH levels are with poor outcomes in many tumors. Rise in LDH plasma concentration tend to have metabolism (anaerobic) involving growth of tumor and metastatic spread, which aid the requirements in conditions of hypoxia. LDH induces inflammatory action on tumor, activating I.L-23 and I.-17 and changing the activity of Arginase-I. It inhibits CD 8+ T L cells and Nk cells, making cells evade the immunity. Raised L.D.H. levels promote tumor angiogenesis, cell migration, and metastatization by inhibiting destabilisation HIF-1 alpha and rise in production of (V.E.G.F.).

LDH is useful in identifying Plasma LDH elevation is tumor-related or not, exploring the biological significance as well as prognostic value of their concordance or discordance. According to previous studies, elevated tissue LDH-A expression is related with elevated Ki-67, high proliferative rates with CNS metastases [6].

The prognostic value of serum LDH level in breast cancer patients has been investigated in various studies [7]. However, it still seems difficult to confirm the prognostic role of Sr. LDH in breast cancer. First, the sample size in some published studies are small. Second, the existing studies are conflicting in their results. Some studies suggested that Sr. LDH was associated with poor prognosis in breast cancer, [7,8,9] whereas other studies have failed to demonstrate such correlations.

Therefore, we can perform a prospective observational study to evaluate the prognostic role of serum LDH in patients with breast cancer.

On the basis of this observation, it would be of great value to prospectively study the prognostic significance of lactate dehydrogenase as tumor marker in carcinoma breast and to find out correlation between stage of breast cancer with serum lactate dehydrogenase levels.

## 2. OBJECTIVES

- ❑ To study the clinical profile of patient with breast cancer.
- ❑ To study the prognostic significance of LDH as tumor marker in breast cancer
- ❑ To compare post-operative LDH level in patient undergoing surgery for breast cancer v/s patient undergoing neoadjuvant chemotherapy
- ❑ Compare variation in preoperative baselines LDH levels and post-operative LDH levels

This is a prospective observational study needed to be carried out in a study group of 90 patients

## 3. METHODOLOGY

It is a prospective observational study done on patients with breast cancer. It will be conducted at Dept. of General Surgery, J.N.M.C and AVBRH, Sawangi (Meghe), Wardha. The study will be conducted on patients with Breast cancer.

TYPE OF STUDY: - Prospective observational study

PLACE OF STUDY: - Acharya Vinoba Bhave Rural Hospital

SAMPLE SIZE: - 90-110 patients needed in the study

1. All newly diagnosed cases of breast cancer will be classified according to TNM staging and will be discussed in tumor board for further management i.e. surgery or Neoadjuvant Chemotherapy.
2. Patient presenting to Surgery out patient department will be examined thoroughly.
3. Patient will be categorized as per inclusion and exclusion criteria.
4. Serum LDH of all these Patient will be evaluated prior to surgery or chemotherapy (NACT)
5. These patients will be classified into post operative and post NACT
6. Repeat testing of LDH will be done in these two group, post operatively on day 1, 7, 14 and on 1 month follow up and post

chemotherapy on day 1 and on 1 month follow up.

7. The preoperative and postoperative LDH level will be studied in operative group, and similar preoperative and postoperative NACT, LDH level will be studied in chemotherapy group.

### 3.1 Study Population

Inclusion Criteria:

- All newly diagnosed cases of breast cancer
- Recurrent breast cancer
- Patients with distant metastasis

Exclusion Criteria:

- Patient who has already undergone mastectomy/ lumpectomy
- Patient who has already underwent Neoadjuvant Chemotherapy
- Patients suffering from Myocardial infarction, Jaundice or Liver disease, polycythemia, Megalo-blastic anemia, hemolytic-anemia, pancreatic-diseases, Rheumatic fever and Tuberculosis were also excluded

All patients admitted with Breast cancer due to any cause will undergo evaluation for participation in the study based on inclusion and exclusion criteria given above.

### 3.2 Initial Evaluation

Detailed demo-graphic profiles will be recorded and complete clinical profile of patient including history of presenting illness, past history, personal history, menstrual and family history will be taken.

### 3.3 Clinical Examination

Proper clinical examination of patient will be performed by examining Bilateral Breast and Axilla along with other systemic examination and pt will be classified according to TNM staging. All routine investigations are sent along with Serum LDH levels. Patients will be classified as those undergoing surgery and those undergoing chemotherapy. Repeat testing of LDH will be done in these two group, post operatively on day 1, 7, 14 and on 1 month follow up and post

chemotherapy on day 1 and on 1 month follow up. The preoperative and postoperative LDH level will be studied in operative group, and similar preoperative and postoperative NACT, LDH level will be studied in chemotherapy group.

### 3.4 Outcome Assessment

The assessment of the outcome will be done at baseline, day 1, 7, 14 and one month follow up in postoperative patients and on baseline, day 1 and one month follow up for post neoadjuvant chemotherapy patients.

### 3.5 Analysis Plan

Analysis will be done with intention to treat principles. All participants with available data at baseline and follow up visits will be included. The impact of missing values will be explored in sensitivity analysis. The data will be entered into the Excel spread sheets and statistical analyses will be conducted using SPSS software. Descriptive analyses of age, sex, and treatment compliance will be performed. The histogram will be plotted to observe the distribution of all the variables and continuous variables which are normally distributed will be described using mean and standard error. The effect size will be expressed in terms of relative risk and risk difference along with their 95% confidence interval.

## 4. RESULTS

With this study we will be able to find out the prognostic significance of serum-Lactate Dehydrogenase as a tumor-marker in Breast cancer i.e raised LDH level are associated with bad prognosis in breast cancer.

## 5. DISCUSSION

Breast cancer is the highly prevalent malignancy and leading cause of death among woman around the world. In India, there is substantial statistically significant increase in breast cancer incidence patterns. During the last two decades, the mortality rates associated with breast cancer also increased. The annual age-standardized rate for BC incidence in India is 25.8/100,000, with a high mortality rate of 12.7/100,000. Breast cancer is clinically, genetically and biochemically heterogeneous. In Asian countries the Prevalence rate of breast carcinoma is

significantly less than in western countries. The incidence of Breast cancer is rising, with the majority of the increase seen in developed countries. India's age-standardized breast cancer incidence rate is one-third that of Western countries. Breast Cancer is the commonest female malignancy world-wide, accounting for almost one fourth of all cancers with an estimated 1.6 Million new cases of cancer diagnosed in 2012. Women from lower developed countries (883, 000 cases) have a significantly higher no. of cases than those from developed countries (794,000) [1,2].

Risk factors that modulate breast cancer development addressed in this analysis include: age, geographical area and socio-economic status, obstetrics history, exo-genous hormones, risk factors in lifestyle (Alcohol, diet, obesity and physical activity), family H/O breast carcinoma, mammography Density, H/O benign breast disease, ionizing-radiation, bone density [3]. A number of studies on carcinoma breast were reported [10-12]. Tanna et. al. endorsed serum lactate dehydrogenase as a prognostic marker in breast cancer [13]. Dighe et. al. reported on assessment of response of neo-adjuvant chemotherapy in patients of carcinoma breast by high frequency ultrasound [14]. Jaggi et. al. focussed on utility of TP53 in breast carcinoma immunophenotypes [15]. Related studies by Laddha et. al [16], Mishara et. al. [17] and Yeola et. al. [18] were reviewed. Khatib et.al. reviewed on Ghrelin for cancer related cachexia [19,20].

Using this study we will try to study the clinical profile of patient with carcinoma breast, the prognostic significance of LDH as tumor marker in breast cancer, compare post-operative LDH level in patient undergoing surgery for breast cancer v/s patient undergoing neoadjuvant chemotherapy, Compare variation in preoperative baselines LDH levels and post-operative LDH levels.

## 6. CONCLUSION

Serum LDH can be used as a tumor-marker in breast cancer

## CONSENT AND ETHICAL APPROVAL

Informed consent will be obtained from all the patients and institutional ethical committee approval, DMIMS (DU) will be taken.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

## REFERENCES

1. Agrawal A, Gandhe MB, Gupta D, Reddy MV. Preliminary study on serum lactate dehydrogenase (LDH)-prognostic biomarker in carcinoma breast. *Journal of clinical and diagnostic research: JCDR*. 2016;10(3):BC06.
2. Malvia S, Bagadi SA, Dubey US, Saxena S. Epidemiology of breast cancer in Indian women. *Asia-Pacific Journal of Clinical Oncology*. 2017;13(4):289-95.
3. Dumitrescu RG, Cotarla I. Understanding breast cancer risk-where do we stand in 2005? *Journal of cellular and molecular medicine*. 2005;9(1):208-21.
4. Liu D, Wang D, Wu C, Zhang L, Mei Q, Hu G, Long G, Sun W. Prognostic significance of serum lactate dehydrogenase in patients with breast cancer: a meta-analysis. *Cancer management and research*. 2019;11:3611.
5. Yashwant R Lamture, Rajesh Domkunti, Avinash Rinait, Mangesh Padmawar. Enterocutaneous fistula in an operated case of total abdominal hysterectomy: A rare case report. *Journal of critical reviews*. 2020;7(8):1085-88.  
DOI:  
<http://dx.doi.org/10.31838/jcr.07.08.227>
6. Pelizzari G, Basile D, Zago S, Lisanti C, Bartoletti M, Bortot L, Vitale MG, Fanotto V, Barban S, Cinausero M, Bonotto M. Lactate dehydrogenase (LDH) response to first-line treatment predicts survival in metastatic breast cancer: First clues for a cost-effective and dynamic biomarker. *Cancers*. 2019;11(9):1243.
7. Petekkaya I, Unlu O, Roach EC, Gecmez G, Okoh AK, Babacan T, Sarici F, Keskin O, Arslan C, Petekkaya E, Sever AR. Prognostic role of inflammatory biomarkers in metastatic breast cancer. *J BUON*. 2017;22(3):614-22.
8. Rajesh Domkunti, Yashwant R. Lamture, Avinash Rinait, Dilip Gode. Breast carcinoma in axillary tail of spence: A rare case report, *Int J Cur Res Rev*. 2020;12(14)(Special Issue);92-95.

- DOI:<http://dx.doi.org/10.31782/IJCRR.2020.9295>
9. Lamture YR, Salunke B. Carcinoma of breast- a study profile, journal of evolution of medical and dental sciences-JEMDS. 2018;7(45):4857-4861. DOI: 10.14260/jemds/2018/1082
  10. Anand, Anupam Surya, Raju Kamlakarrao Shinde. To compare the effects of adjuvant and neoadjuvant chemotherapy on outcome of stage III carcinoma breast. Journal of Evolution of Medical and Dental Sciences-JEMDS. 2020;9(8):496-501. Available:<https://doi.org/10.14260/jemds/2020/112>
  11. Gupta V, Deshpande P, Bhake A. DNA methylation and its correlation with breast cancer pathological prognostic staging. Journal of Molecular Diagnostics. 2019;21(3)S:S18-19.
  12. Mudey A, Nayak S, Khapre M, Goyal R. Reaching out to rural women to screen for breast cancer: A step to reduce the burden of breast cancer in a rural area of central India. European Journal of Cancer. 2016;57(2):S25.
  13. Tanna Hardik, Bakane BC. Serum lactate dehydrogenase as a prognostic marker in breast cancer. Journal of Evolution of Medical and Dental Sciences-JEMDS. 2015;4(91):15612-14. Available:<https://doi.org/10.14260/jemds/2015/2243>
  14. Dighe, Sajika Pramod, Raju K Shinde, Sangita Jogdand Shinde, Anupam Anand. Review on assessment of response of neo-adjuvant chemotherapy in patients of carcinoma breast by high frequency ultrasound. Journal of Evolution of Medical and Dental Sciences-JEMDS. 2020;9(51):3873-80. Available:<https://doi.org/10.14260/jemds/2020/849>
  15. Jaggi Ria, Samarth Shukla, Sourya Acharya, aSunita Vagha. Utility of TP53 in breast carcinoma immunophenotypes. Journal of Clinical and Diagnostic Research. 2020;14(9). Available:<https://doi.org/10.7860/JCDR/2020/44743.14049>
  16. Laddha, Ankita Gajanan, Samarth Shukla, Ravindra P Kadu, Arvind S Bhake, Sunita Vagha, Miheer Jagtap. Histopathological types of benign proliferative lesions in peritumoural vicinity of carcinoma breast. Journal of Clinical and Diagnostic Research. 2020;14(5):EC21-26. Available:<https://doi.org/10.7860/JCDR/2020/43291.13701>
  17. Mishra Preeti, Sunita Vagha, Samarth Shukla, Sourya Acharya, Aditi Goyal. Assessment of cytokeratin expression in carcinoma breast. Journal of Evolution of Medical and Dental Sciences-JEMDS. 2020;9(35):2545-49. Available:<https://doi.org/10.14260/jemds/2020/553>
  18. Yeola, Meenakshi Eknath, Aditya Prabhakar Rao Borgaonkar. Chemotoxicity in carcinoma breast patients- its incidence and trends in severity- an observational study. Journal of Evolution of Medical and Dental Sciences-JEMDS. 2021;10(10):667-72. Available:<https://doi.org/10.14260/jemds/2021/144>
  19. Khatib, Mahalaqua Nazli, Anuraj H. Shankar, Richard Kirubakaran, Abhay Gaidhane, Shilpa Gaidhane, Padam Simkhada, Zahiruddin Quazi Syed. Ghrelin for the management of cachexia associated with cancer. Cochrane Database of Systematic Reviews. 2018;2. Available:<https://doi.org/10.1002/14651858.CD012229.pub2>
  20. Khatib, Mahalaqua Nazli, Abhay Gaidhane, Shilpa Gaidhane, Zahiruddin Quazi Syed. Ghrelin as a promising therapeutic option for cancer cachexia. Cellular Physiology and Biochemistry. 2018;48(5):2172-88. Available:<https://doi.org/10.1159/000492559>

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