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**Authors' Affiliation:**
1. Institute of Molecular Biology and Biotechnology (IMBB), The University of Lahore – Pakistan
2. National Institute for Genomics and Advanced Biotechnology (NIGAB), National Agricultural Research Centre (NARC), Islamabad – Pakistan
3. Institute of Nuclear Medicine and Oncology, Lahore – Pakistan
4. Department of Biotechnology, University of Sargodha, Sargodha - Pakistan

**\*Corresponding Author:**
Imran Riaz Malik
Email:
imran.riaz@uos.edu.pk

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# Study of diagnostic and prognostic parameters in Breast cancer patients without metastasis

Aqsa Neelam[1], Ahmad Ali[2], Rabail Alam[1], Ghulam Mujtaba[3], Imran Riaz Malik[4]*

## Abstract

**B**ackground: Carcinoma of the breast is the most prevalent cause of mortality from cancer in women aged 40-69 years. The aim of the present study was to examine any alteration in the status of lactate dehydrogenase, ferritin, gamma glutamyl transferase, Platelets, hemoglobin, alkaline phosphatase, aspartate transaminase, alanine transferase and bilirubin in the plasma of breast cancer patients without distant metastasis, to establish their diagnostic and prognostic values.

Methods: Current reading describes a study conducted on 50 breast cancer patients from Institute of Nuclear Medicine and Oncology (Lahore). The patients were clinically categorized as stage II (19 patients) and stage III (29 patients) respectively. Most of the patients were diseased with infiltrative ductal carcinoma (48) of the breast. Blood samples of all patients were collected after forty days of chemotherapy course besides 10 healthy subjects.

Results: There was a significant rise in LDH (221.48 ± 18.44) and Ferritin (356.46 ± 12.28) levels as compared to control groups. Concentration of GGT (34.12 ± 1.61) was also elevated but not significantly raised. There was no significant rise in ALP (279.27 ± 26.60), AST (49.44 ± 8.510), ALT (33.40 ± 2.83), bilirubin (4.87 ± 3.96), Hb (11.16 ± .299) and platelets (032.54 ± 21.68) levels in comparison to normal control subjects. An elevation of LDH and ferritin levels in cases of carcinoma breast signifies its importance as a biomarker of disease. A serial measurement of these enzymes would have diagnostic and prognostic significance and help treatment decisions.

Conclusion: The ferritin along with lactate dehydrogenase can be used as a valuable biomarker for breast cancer diagnosis and prognosis.

## Introduction

Breast cancer is perhaps the most frequently diagnosed cancer in females plus a major cause of cancer moralities worldwide [12]. The breast cancer is the most frequently occurring in developed and developing countries with an estimation of 690,000 new cases in each region [2]. In 2008 there was an estimation of 23% (1.38 million) of total new cancer cases and 14% (458,400) of the total cancer deaths. The incidence rate of breast cancer has been sharply decreased in some of these countries including the United States, United Kingdom, France and Australia and has also been decreasing in North America and many European countries. The breast cancer incidence and mortality rates have been increasing in many African and Asian countries including Uganda, South Korea, and India [12].

The incidence rate of breast cancer is highest in Pakistan than any other Asian country. In Western population breast cancer is common at older age but in Pakistan it is more common at young age and maximum patients are represented with later stages of cancer (Stage 3 and 4) [3]. A 50 year age-cut point is found effective in assessing prognostic factor in breast cancer [10]. In Pakistan, there is estimation of 90000 new cases and 40000 breast cancer related deaths annually. It is estimated that one out of nine Pakistani women is likely to suffer from breast cancer [13].

Tumor markers are substances produced by the cancer cells or other cells of body in response to cancer or other noncancerous conditions. These are found in blood, stool, other body fluids, or tissues of some patients with cancer. Tumor markers may be used in diagnosis, prediction of patient's response to treatment or determine whether cancer has returned [7]. The stage IV patients were determined through lymph node evaluation that can provide important prognostic information [16]. There is high need to investigate further tumor markers for diagnosis and treatment management of cancer. Moreover, such simple, affordable and practicable biochemical tests are needed because the analytical methods of many existing tumor marker tests are unapproachable for general population as the facilities for these are available at only sophisticated and well equipped centers with latest technology. The present study is undertaking to assess the clinical utility of certain biochemical investigations that include LDH, GGT, Ferritin, HB, platelets, ALP, AST, ALT, and bilirubin, to find out useful biomarker (s) that may help in breast cancer diagnosis and prognosis.

## Methods

Fifty breast cancer victims that were admitted to the institute of nuclear medicine and oncology, Lahore were included in this study. To direct the research an endorsement of host Institutional Bioethics Committee was taken. Out of 50 patients, 24% of patients were diagnosed with invasive ductal carcinoma. Only 1% of patients had medullary and invasive lobular carcinoma. The age of the patients was in the range of 28-64 years. The patients were clinically categorized as stage 2 (19) and stage 3 (29), respectively. A questionnaire was designed to obtain the information of breast cancer patients including patient's name, age, marital status, duration of disease, duration of treatment, family history of breast cancer, history of mastectomy, and past medical history. Clinical data of patients was obtained from patient's files. An informed consent was held and 20 control subjects were also enrolled. The age group of control subjects was within the range of 25-45. Entire research work was conducted in biochemical lab of the institute of nuclear medicine and oncology. Blood samples (5ml) were collected with the help of expert technicians and consent of patients. Serum from blood samples were separated by centrifugation at 3000rpm for 10 minutes and stored at -20ºC prior to processing.

Twelve biochemical parameters were analyzed in this study by using enzyme kits. These parameters included, hemoglobin (Hb), platelets, white blood cells (WBCs), alkaline phosphatase (ALP), alanine transferase (ALT), aspartate aminotranferase (AST), bilirubin, blood urea nitrogen (BUN), creatinine, lactate dehydrogenase (LDH), ferritin and gamma glutamyl transferase (GGT). The obtained data was analyzed by using software statistical package for The Social Science (SPSS Version 13). Frequency and descriptive analyses were used to describe the data. Student T test was also used to differentiate between two numerical data.

## Results

**Patient's characteristics:** 50 breast cancer patients (Stage 1, 2, 3) and 10 control subjects were studied. The age of patients was ranged between 28 and 64. 13.5 % of patients were suffering from disease for more then 1-2 years and 11.5 % for less than 3-9 months. Out of 50 patients, 11 patients had family history and 39 patients had no family history. Majority of patients were histologically identified with invasive ductal carcinoma (IDC). 14.5% of patients had been mestectomized. The general patient characteristics are shown in Table 1.

| General characters | No. of cases | Percentage (%) |
|---|---|---|
| **Age (years)** | | |
| 28-40 | 19 | 9.5 |
| 41-50 | 17 | 8.5 |
| 51-64 | 14 | 7 |
| **Disease duration** | | |
| >1-2 (years) | 27 | 13.5 |
| <3-9 (month) | 23 | 11.5 |
| **Family history** | | |
| Positive | 11 | 5.5 |
| Negative | 39 | 19.5 |
| **Histologic type** | | |
| IDC | 48 | 24 |
| ILC | 1 | .00095 |
| Medullary | 1 | .00095 |
| **Stage of tumor** | | |
| Stage 1 | 0 | 0 |
| Stage 2 | 31 | 15.5 |
| Stage 3 | 19 | 9.5 |
| **Cancer site** | | |
| Left | 18 | 9 |
| right | 32 | 16 |
| **Surgery** | | |
| Yes | 29 | 14.5 |
| No | 21 | 10.5 |
| **Receptor Status** | | |
| Positive | 17 | 8.5 |
| Negative | 33 | 16.5 |

**Table 1:** Demographic and general health indicators of Patients

**Serum ferritin in breast cancer:** The results are summarized in table 2. After statistical analysis it has been cleared that the control subjects had the mean serum ferritin concentration of 263.60 ng/l. The women with breast cancer had mean ferritin concentration of 356.46 ng/l with standard deviation of 86.87. The difference between the means of two groups (control, patients) is significant (P<0.005). However there was no difference in serum ferritin in different stages of cancer.

**Serum LDH in breast cancer:** Serum LDH levels were also raised in cancer patients then the control group. The mean LDH value was 221.48 with standard deviation of 130.37 in cancer group. And the mean serum LDH concentration in control subjects was 346.20. So the LDH concentration was significantly higher in breast cancer patients (P<0.005) then the healthy controls.

**Serum GGT in breast cancer:** The statistical analysis of data showed that there was no significant difference (P>0.005) in GGT concentration in both the control and patients groups. The results of both groups were in normal range.

**Liver functioning tests (LFT'S) in breast cancer:** There was no significant difference (P>0.005) in the concentrations of ALP, AST, ALP, bilirubin between breast cancer patients (stage0-III) and healthy controls.

**Hematological parameters in breast cancer:** The hematological parameter hemoglobin was in normal range in breast cancer patients. Platelets were in raised concentration in many patients but statistically there was no significant difference (P>0.005) in Hb and platelets concentrations between healthy controls and breast cancer patients.
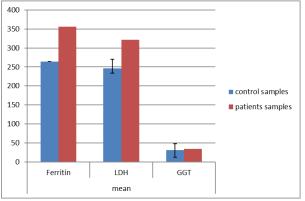


**Figure 1:** A representation of statistically significant biochemical parameters (ferritin and LDH) showing higher ferritin and lactate dehydrogenase concentration in cancer patients in comparison to healthy females (i.e. P<0.005).
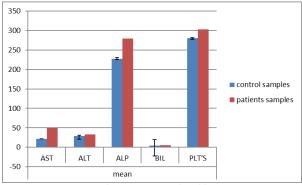


**Figure 2:** Comparison between control and breast cancer groups for measured biochemical parameters AST, ALT, ALP, and platelets (PLT).

## Discussion

In the present study, mean levels of lactate dehydrogenase was 346.20 ± 55.06 U/L, 221.48 ± 130.37 U/L in controls and breast cancer patients respectively. The mean values of lactate dehydrogenase were found significantly raised, when compared to controls. There was significant rise (P<0.005) in LDH levels in breast cancer as compared to healthy subjects (fig. 1). The results of our study are in congruent with Mishra who estimated the serum LDH in 102 breast cancer patients and find it to be elevated [14].

Fentimen and Allen also reported a similar increase of serum LDH. They had done a study on 96 breast cancer patients [8]. Our findings were similar to the study by Chandrakanth who reported a significant increase in LDH in his study of 60 breast cancer patients [5]. Seth and his colleagues, in a study involving 25 breast cancer patients also determined significantly higher values of serum LDH [15].

In our study the mean values of serum ferritin was 263.60 ± 74.00 and 356.46 ± 86.87 in healthy females and carcinoma breast respectively. The serum ferritin was significantly elevated in breast cancer as compared to healthy subjects (fig. 1). Our findings of serum ferritin are in agreement with the results of study carried out by

| Parameters | Mean ± S.E (range) | | P-value |
| --- | --- | --- | --- |
| | Patient group | Control group | |
| Ferritin | 356.46 ± 12.28) (37-432) | 263.60 ± 23.40 (166-403) | **<0.005** |
| LDH | 221.48 ± 18.44 (210-477) | 346.20 ± 17.41 (275-423) | **<0.005** |
| GGT | 34.12 ± 1.61 (17-56) | 30.70 ± 2.47 (19-42) | **>0.005** |
| ALP | 279.27 ± 26.60 (146-1127) | 227.7 ± 15.05 (176-336) | **>0.005** |
| AST | 49.44 ± 8.510 (15-345) | 21.7 5 ±.1.87 (13-34) | **>0.005** |
| ALT | 33.40 ± 2.83 (10-114) | 29.0 ± 2.36 (16-40) | **>0.005** |
| Bilirubin | 4.87 ± 3.96 (0.5-1.3) | 4.54 ± .26 (3.5-5.8) | **>0.005** |
| BUN | 10.79 ± .81 (0.6-31.7) | 12.7 ± 1.08 (7-18) | **>0.005** |
| Creatinine | 1.03 ± .22 (0.7-1.3) | 0.9 ± .05 (0.7-1.1) | **>0.005** |
| Hemoglobin | 11.16 ± .40 (9.5-11.9) | 11.59 ± .35 (10-13.7) | **>0.005** |
| Platelets | 302.54 ± 21.68 (57-70) | 280.9 ± 25.63 (207-396) | **>0.005** |

**Table 2:** Comparison of biochemical parameters in both patients and control groups highlighting significant P-values (<0.005) for Ferritin and LDH.

| Group | LDH/Ferritin (Mean ± S.D) |
| --- | --- |
| Patient | 2.67 ± 2.67 |
| Control | 1.310 ± 0.39 |

**Table 3:** Mean value ratio (LDH/Ferritin) in non-metastatic breast cancer patients and control group

Jacobs and his colleagues who witnessed a significant increase in serum ferritin concentration in carcinoma breast patients [11]. Cujic evaluated the 57 breast cancer patients for serum ferritin and he also found that ferritin concentration was raised in breast carcinoma patients [6]. Bilirubin and ALP are not significantly raised ($P>0.005$) in our study. Our study results are similar to Anuradha's study. She also found that ALP and bilirubin levels were not raised in breast carcinoma, when compared to controls [1]. Mishra also assessed that the level of heamoglobin and ALP in breast carcinoma patients was not significantly higher and coincides with our analysis where we also found that there was no substantial increase in serum Hb and ALP in breast cancer patients as compared to controls [14]. There is also a link with another study in which 249 breast cancer patients were tested for serum Hb, and no substantial increase was found compared to controls [3].

Our findings were similar to Veni, who reported that there was no significant rise in bilirubin concentration as compared to controls [17]. The results of Cao and Wang study also correlates with our study. He found that ALT, AST and ALP concentrations were not significantly raised in breast cancer patients without distant metastasis as compared to breast cancer patients with liver metastasis [4].

It was concluded from this study that ferritin along with lactate dehydrogenase can be used as a useful biomarker for the diagnosis and prognosis of breast cancer.

## Authors' Contribution

AN conducted the research, AA help in drafting and data analysis, GM helped in field and lab work, RA did data analysis, IRM help in designing study, drafting, and final draft.

## Competing interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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