

Evaluation of biochemical marker serum LDH and Gamma GT in breast cancer patients**Meenal Vaidya Rajput¹, Ravi Kant Sharma², Vandana Varma³, Teena Agrawal⁴, Shreya Nigoskar⁵**¹*Demonstrator, Department of Biochemistry, MGM Medical College, Indore, Madhya Pradesh, India*²*Assistant Professor, Department of Biochemistry, School of Medical Sciences and Research, Greater Noida, India*³*Associate Professor, Department of Biochemistry, MGM Medical College, Indore, Madhya Pradesh, India*⁴*Assistant Professor, Department of Biochemistry, Index Medical College & Research Centre Indore, Madhya Pradesh, India*⁵*HOD, Department of Biochemistry, Index Medical College & Research Centre Indore, Madhya Pradesh, India***Received: 28-04-2021 / Revised: 16-06-2021 / Accepted: 20-07-2021****Abstract**

Background: Breast cancer is the second most common malignancy related mortality in women worldwide. Multiple factors including genetics, lifestyle factors and socioeconomic etc. are associated with an increased risk of developing breast cancer. For the early detection of breast cancer a number of biochemical markers have been studied to evaluate the malignancy. **Aim:** To analyse serum Lactate Dehydrogenase, Gamma Glutamyl Transpeptidase, liver enzymes (SGOT, SGPT, & ALP) and total proteins in diagnosis of carcinoma breast patients and compared with controls. And evaluate the relationship of serum LDH, GGT levels with ALP of carcinoma breast patients of post-menopausal age group. **Materials & Methods:** The serum biochemical markers were estimated in 60(30-premenopausal women, 30-post menopausal women) clinically and histopathologically confirmed patients with carcinoma breast and 60 number of healthy age- matched individuals served as control. Lactate dehydrogenase (LDH), Serum Gamma Glutamyl Transpeptidase (GGT) and Alkaline phosphatase (ALP) were analysed and estimated. The statistical analysis was done by using SPSS software. The results were expressed as Mean±SD. The student's paired 't'-test was carried out for comparison of data & p-value <0.005 was considered statistically significant. **Results:** The mean serum LDH, GGT, and ALP activities in patients with carcinoma breast were significantly (p<0.0001) increased as compared to controls, and a steady increase was observed in their levels from premenopausal to post-menopausal women. **Conclusion:** In this study, it is too suggests that the estimation of less specific biomarkers like LDH, GGT, and ALP can be used as routine screening tests in all suspected carcinoma breast patients because these are less expensive and easily assayed and used for diagnosing breast cancer, detecting metastasis and monitoring the cancer progression and treatment.

Keywords: Breast cancer, Lactate Dehydrogenase, Serum Gamma Glutamyl Transpeptidase, Alkaline phosphatases.

This is an Open Access article that uses a fund-ing model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Cancer incidence is increasing in India as well as on a global basis. According to World Health Organisation, an estimated 19.3 million new cancer cases and almost 10.0 million cancer deaths occur in 2018 [1]. Furthermore, female breast cancer has surpassed lung cancer as the most commonly diagnosed cancer, with 2.3 million new cases (11.7%), followed by lung (11.4%), colorectal (10.0%), prostate (7.3%), and stomach (5.6%) cancers. Such a burden of the disease accounts for a significant proportion of annual health care spending worldwide [2]. Breast cancer is now the most common cancer in all urban areas in India, and 2nd most common in the rural areas [3]. Breast cancer is a malignant proliferation of epithelial cells lining the ducts or lobules of the breast. Human breast cancer is a colonial disease [4]. A single transformed cell is the product of a series of somatic (acquired) or germ line mutations is eventually able to express full align ant potential [5]. Many experimental, clinical and epidemiological studies have revealed that a number of factors influence breast cancer etiology. Hormonal factors, reproductive factors, genetic factors, lifestyle, and dietary factors [6].

Primary prevention of breast cancer is still not available except by extreme measures such as a prophylactic mastectomy for women who are genetically at high risk, so efforts to promote early detection continue to be the major focus in fighting breast cancer. The goal of early detection is to diagnose and treat breast cancer patients at an early stage when the prognosis for long-term survival is best. Prognosis is generally more favourable for women with an early-stage disease than for those with more advanced disease as early detection is associated with decreased mortality [7]. For the early detection of carcinoma of various origins, a number of biochemical markers have been studied to evaluate the malignancy [8].

Serum LDH enzyme is required for anaerobic glycolysis. A rapid increase in number of malignant cells modulates the LDH level in cytoplasmic compartment of cells, due to upregulation in its gene [8]. It leads to increase in serum LDH level in breast cancer patients. This increased LDH level is helpful for fulfilment of metabolic requirements and anaerobic glycolysis of these malignant cells. The value of serum LDH was found to be specific in patients with breast malignancy and also corresponds with clinical TNM staging, while patients with benign breast disease such as fibroadenomas have LDH value close to carcinoma [9]. LDH activity correlates with tumor burden, and the metastatic BC exhibits elevated LDH level than normal breast tissue. The increased level of LDH induces reduce

*Correspondence

Dr. Teena Agrawal

Department of Biochemistry,

Index Medical College & Research Centre Indore India.

E-mail: teenamanoj101283@gmail.com

treatment responsiveness.LDH may also be considered as an indicator of tumor progression [10]. Gamma Glutamyl transpeptidase (GGT) is an enzyme of glutathione metabolism, involved in cell's detoxification pathway and apoptotic balance-including tumor development,progression and chemotherapy resistance [11].ALP is a serum enzyme whose overall concentrations represent the combined action of many isoenzymes located in the lining of the liver, bone, kidney, and intestines.This skeletal isoenzyme is derived from osteoblasts and,as bone repair actions,for instance with bone metastases causes the release of significant quantities of the enzyme [11]. Increased levels of serum ALP are correlated to poor prognosis in certain cancers [12].

Some researchers have also shown that an elevated level of serum ALP has been reported in patients with breast cancer and has been frequently proven to indicate liver and bone metastases [13].

Aims and Objectives

The present study was aimed to evaluate and estimate the certain biochemical investigations like serum Lactate dehydrogenase, Gamma Glutamyl Transpeptidase, Alkaline phosphatase, liver enzymes (SGOT, SGPT, & ALP) and total proteins in diagnosis of carcinoma breast patients and compared with controls. And evaluate the relationship of serum LDH, GGT levels with ALP of carcinoma breast patients of post-menopausal age group.

Materials and Methods

The present study was carried out in the Department of Biochemistry, Index Medical College & Research Centre, Indore (M.P.) during the period of Feb 2019 to Jan 2020 after approval from the ethical committee of the institute. Total 120 subjects were

included in this study, which was categorized into two groups cases and controls(60 cases and 60 controls).The present study was undertaken to determine biochemical changes in 60 carcinoma breast cases.60 cases were divided into 2 groups premenopausal 30 and postmenopausal 30 cases, which were newly diagnosed and untreated. These values are compared with age and sex matched 60 healthy controls. 5 ml blood samples were obtained from ant. cubital vein of upper limbs of each patient and controls. The consent was obtained both from cases and controls. Serum was separated and analysed by using standard methods.

Inclusion criteria

All patients who were recently diagnosed as carcinoma breast clinically and histopathologically confirmed.

Exclusion criteria

Carcinoma breast associated with concomitant pathology like DM, HTN, renal failure and severely ill patients.

Observation and Results

All data were analyzed using SPSS statistical software. Results are expressed as mean ± standard deviation. Student paired ‘t’ test was used to compare the values. Differences with a ‘p’ value less than 0.005 were considered to be statistically significant.

In this study, LDH, GGT, ALP, Total Protein levels are increased significantly in CA breast patients, when compared to controls, but further increased in CA breast cases of post-menopausal age group. Albumin levels are decreased significantly in CA breast patients, when compared to controls, but further decreased in CA breast cases of post-menopausal age group.

Table 1: Comparison of biochemical parameter between cases and controls

S. No.	Parameter	Controls	Cases (premenopausal)	Cases (postmenopausal)	p-value
1	LDH(U/L)	285.11±38.07	528.43±31.97	738.43±68.04	<0.0001[HS]
2	GGT(IU/L)	23.66±7.23	48.87±12.90	81.45±14.88	<0.0001[HS]
3	ALP(IU/L)	40.23±16.37	124.23±24.09	186.01±22.64	<0.0001[HS]
4	Total Protein(g/dl)	6.891±0.795	7.372±1.893	8.989±1.224	<0.0001[HS]
5	Albumin(g/dl)	4.771±0.213	2.689±0.589	2.333±0.432	<0.0001[HS]
6	Globulin(g/dl)	2.932±0.291	5.323±0.567	5.320±0.523	<0.0601[NS]
7	SGOT(U/L)	35.15±20.12	63.90±15.23	67.11±13.45	<0.0001[HS]
8	SGPT(U/L)	37.45±18.98	69.77±16.90	69.99±16.56	<0.0001[HS]

Table 2: Pearson correlation coefficient r-value in postmenopausal patients

S.No.	Parameter	r-value
1.	LDH	+0.1018
2	GGT	-0.2131

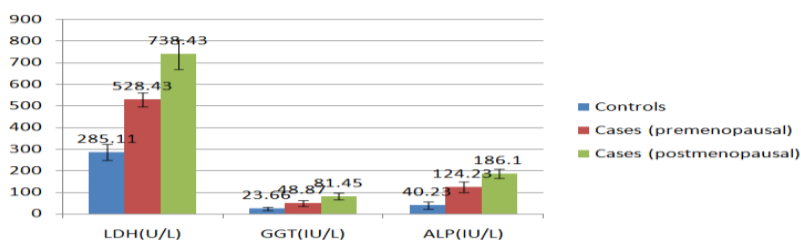


Fig1: Comparison of LDH, GGT and ALP in cases and controls

Correlation of ALP with LDH and GGT in postmenopausal patients

Discussion

In present study serum LDH is significantly (p<0.001) increased in CA breast patients (mean 528.43±31.97) when compared to controls (mean 285.11±38.07) but further increased in CA breast cases of post-menopausal age group (mean 738.43±68.04). It is due to induction of LDH synthesis in normal tissues of the host by invading tumour causes release of intracellular enzymes so aggressiveness of its tumour growth directly correlates with serum LDH levels and act as a diagnostic and prognostic marker in CA breast patients. Serum

LDH levels in CA breast patients of post-menopausal age group is positively correlated with ALP (r = + 0.1018). The present study correlates with Swetha et aland Kher et al[14]. Our findings correlate with the study of Shrivastav et al [15], Chandrakanth et al [16], who found the mean serum LDH levels are significantly elevated in breast cancer patients. The findings of this study are reflected by the findings of Sandhya mishra et al [17], which have shown that breast carcinoma patients with and without metastasis have higher serum lactate dehydrogenase levels.Serum GGT is significantly (p<0.001)

increased in CA breast patients (mean 48.87 ± 12.90) when compared to controls (mean 23.66 ± 7.23) but further increased in CA breast cases of post-menopausal age group (mean 81.45 ± 14.88). It may be due to response of increased reactive oxygen production in the blood [18]. Serum GGT level in CA breast patients of post-menopausal age group is negatively correlated with ALP ($r = -0.2131$). The present study correlates with Seth and Chowdary et al [13]. A study by Jarari et al [19] reported significantly higher level of serum GGT in breast cancer cases as compared to controls, but the significant spike was observed in the premenopausal group when compared with that of postmenopausal. In contrast to our study, increased GGT level was observed in postmenopausal breast cancer patients as compared to premenopausal age group. Findings of the present study are similar to that of Sandhya Mishra et al [17] who reported a significant increase in serum Gamma glutamyl transferase levels in breast cancer. Serum ALP levels (mean 124.23 ± 24.09) is significantly increased ($p < 0.001$) in CA breast patients when compared with controls (mean 40.23 ± 16.37) but further increased in CA breast cases of post-menopausal age group (mean 186.01 ± 22.64) it may be due to neoplastic metastasis of the liver resulting from localised intra hepatic cholestasis with increased synthesis of enzyme in liver tissue [20]. The present study correlates with Sandhya Mishra et al [18]. In contrast to this study Priya Mehta et al [10], did not find any significant difference in ALP levels in non-metastatic breast cancer. The present study was undertaken to evaluate the role of Lactate dehydrogenase and Gamma glutamyl transferase and alkaline phosphatase in breast cancer patients and to assess their value in early detection, monitor therapy and progression. The study was consistent with findings of a multitude of other studies which have shown elevations of serum Lactate dehydrogenase in breast cancer. Serum total proteins was significantly ($p < 0.001$) increased and serum albumin was significantly decreased ($p < 0.001$) in CA breast cases but within normal range when compared to controls but further increase of serum total proteins and further decrease of serum albumin is observed in postmenopausal patients. During the process of tumour growth certain tissue proteins are released in to the circulation so serum total protein concentration increased. Hypoalbuminemia is due to oxidative stress, enhancement in their catabolism rather than synthesis. SGOT and SGPT is also significantly ($p < 0.001$) increased in CA breast patients when compared to controls because of accelerated de novo synthesis of the enzyme and subsequent regulation in the serum.

Conclusion

The present retrospective study has shown a significant association between the serum LDH and Gamma GT levels in cases diagnosed with carcinoma breast especially in postmenopausal women. As per the present study aggressiveness of breast cancer has been seen in post-menopausal patients and accounts for high morbidity and mortality. Serum ALP is significantly increased in total CA breast patients but further more increased in post-menopausal patients. ALP is a potential marker for early detection of cancer with and without metastasis that helps to diagnose the people in developing countries. Serum total proteins are significantly increased and albumin is decreased in CA breast patient but more markedly increase total proteins and decrease albumin was seen in post-menopausal patients, due to oxidative stress. Our study suggests that the estimation of less specific biomarkers like LDH, GGT, and ALP can be used as routine screening tests in all suspected carcinoma breast patients because these are less expensive and easily assayed and used for diagnosing breast cancer, detecting metastasis and monitoring the cancer progression and treatment.

References

1. Sung H, Laversanne M, Soerjomataram I, Jemal A et al. Global Cancer Statistics 2020: GLOBOCON Estimates of Incidence

- and Mortality Worldwide for 36 Cancers in 185 Countries. *A Cancer journal for Clinicians*. 2021;71(3):1
2. Knudson AG Jr. Mutation and cancer: statistical study of retinoblastoma. *Proc Natl Acad Sci U S A*. 1971;68(4):820-3
 3. Phaneendra D S, Deepak and Mahmood. Serum ferritin, lactate dehydrogenase, and gamma glutamyl transferase levels in patients with breast carcinoma *International Journal of Clinical Biochemistry and Research* 2021;8(1):40-47.
 4. Baloch AH, Ahmed M, Ahmad A, Tareen M, et al. Various Aspects, Patterns and Risk Factors in Breast Cancer Patients of Balochistan. *Asian Pac J Cancer Prev*. 2012; 13(8):4013-6.
 5. Cao R, Wang LP. Serological diagnosis of liver metastasis in patients with breast cancer. *Cancer Biol Med*. 2012;9(1):57.
 6. Curado MP, Shin HR. *Cancer Incidence in Five Continents Lyon: World Health Organization and International Association of Cancer. International Agency for Research on Cancer*. 2013; 9(5):2
 7. Zahra A., Ahmed, Abdrabo. Assessment of the Activity of Lactate Dehydrogenase, Gamma-glutamyl Transpeptidase. *Gezira Journal of Health Sciences*. 2019; 15(1):1
 8. Aditi Agrawal et al., LDH Biomarker in Ca. *Breast Journal of Clinical and Diagnostic Research*. 2016;10(3): BC06-BC08
 9. Koukourakis MI, Sivridis E, Liberis V. Serum and tissue LDH levels in patients with breast/gynaecological cancer and benign diseases. *Gynecol Obstet Invest*. 2009;67(3):162-68
 10. Mehta P, Rupala N, Rawat S, Goswami G.K. Study on role of ALP, LDH and Lipase as prognostic markers in female breast cancer patients of Saurashtra region of Gujarat. *Indian Journal of Applied Research* 2021;11(01)
 11. Basnyat AS, Jha A, Pathak R, Shrestha BG. Study of Serum Lactate Dehydrogenase and Gamma-Glutamyl Transpeptidase in Breast Cancer Patients Receiving Chemotherapy. *J. Trop. Life. Science*. 2017; 7 (2): 128 – 132.
 12. Wei, X. L., Wang, D. S., Zhou, Y. X. et al. The predictive value of alkaline phosphatase and lactate dehydrogenase for overall survival in patients with esophageal squamous cell carcinoma. *Tumour Biology: the Journal of the International Society for Oncodevelopmental Biology and Medicine*. 2016; 37(2), 1879–1887.
 13. Choudhari A., Desai P., Indumati V., & Kadi S. Activities of serum ADA, GGT and ALP in carcinoma breast—a case control study for diagnostic and prognostic significance. *Indian Journal of Medical Sciences*. 2013; 67(5-6), 123-129
 14. Swetha et al and Kher et al Serum Lactate Dehydrogenase and Lipid Profile in Breast Cancer *IJPBS*. 2013; 3(2): 423-43.
 15. Shrivastava, V., Meena, P., Nandwani, R., Meena, S. A study of Serum levels of LDH and ALP in carcinoma breast: An Observational study. *Journal of Dental and Medical Sciences (IOSR-JDMS)*. 2016; 15(9), 26-31.
 16. Nagaraj C., Jayaprakash Murthy S., & Pyati A. Study of serum levels of gamma-glutamyl transferase, lactate dehydrogenase, malondialdehyde and vitamin-E in breast cancer. *International Journal of Pharmacy and Biological Sciences*. 2011; 2(4).
 17. Mishra, S., Sharma, D. C., & Sharma, P. Studies of biochemical parameters in breast cancer with and without metastasis. *Indian Journal of Clinical Biochemistry*. 2004; 19(1), 71-75.
 18. Rosalki SB. Gamma-glutamyl transpeptidase. *Adv Clin Chem*. 1975; 17:53-107.
 19. Jarari AM, Shakila S, Alsoaieiv SO. Serum levels of LDH and gamma GT in Libyan breast cancer patients. *Indian Journal of Applied Research*. 2013; 3 (12): 32-34.
 20. Kaplan MM. Alkaline phosphatase. *Gastroenterology*. 1972; 62: 452-68.

Conflict of Interest: Nil Source of support: Nil