Original Research Article

Study of serum LDH and GGT levels in carcinoma breast

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Abstract

Background: Breast cancer is the second most common cancer in women next only to cervical cancer. Multiple factors are associated with an increased risk of developing breast cancer. For the early detection of carcinoma of breast, 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.
Material & Methods: The serum biochemical markers were estimated in 60(30-premenopausal women, 30-post menopausal women) clinically and histopathological confirmed patients with carcinoma breast and 40 number of healthy age- matched individuals served as control. Lactate dehydrogenase (LDH) Serum Gamma Glutamyl Transpeptidase (GGT), were analysed and estimated. Statistics: Data was analysed with student's paired 't'-test was determined.
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 to suggest that the estimation of LDH, GGT, and ALP can be used as routine screening tests in all suspected carcinoma breast patients and for general population and can detect metastasis.
Keywords: Lactate Dehydrogenase, Serum Gamma Glutamyl Transpeptidase, Fine Needle Aspiration Cytology, Alkaline Phosphatase.

1. Introduction

In India breast cancer is the second most common cancer in women next only to cervical cancer [1]. Highest incidence of breast cancer is seen in the 45- 49 yrs. age group. Multiple factors are associated with an increased risk of developing breast cancer these can be genetic, environmental & histological factors.

Genetic factors are estimated to cause 5 to 10% of all breast cancer cases. It occurs more commonly in women with a family history of breast cancer and is due to mutation in the breast cancer susceptibility genes BRCA1 and BRCA2 [2,3]. BRCA1 is a tumour suppressor gene located on chromosome 17 (17q21) and accounts for 40% of familial breast cancer. BRCA2 is located on chromosome 13(13q12-13) and accounts for about 30% of familial breast cancer [4].

Major environmental factors [5] are mainly related to the exposure of women to circulating estrogens such as early menarche, nulliparity, short lactation period, late menopause, hormone replacement therapy[6], diet high in fats and obesity. Non hormonal risk factors include exposure to radiation and alcohol consumption.

Cancer of the breast affects the left slightly more often than the right. Upper outer quadrant of the breast is the most common location. Breast cancer may arise from the epithelium of the duct system anywhere from the nipple end of the major lactiferous ducts to the terminal duct unit [7], which is in the breast lobule. Breast cancers are classified into those that have not penetrated the basement membrane (non-invasive) ductal carcinoma in situ, Lobular carcinoma in situ and those that have (invasive) infiltrating invasive ductal carcinoma, invasive lobular carcinoma, medullary carcinoma, and colloid carcinoma [8].

Histological factors [9] are based on breast tissue biopsy. Proliferative benign diseases of the breast, atypia and in situ carcinoma increase the risk of development of invasive carcinoma in the future.

Any patient who presents with a breast lump or other suspicious symptoms of carcinoma like nipple changes, retraction or discharge or axillary mass the diagnosis should be made by clinical examination, imaging techniques like mammography ultrasonography &MRI and biopsy FNAC.

Most widely used system for staging of breast cancer is American joint committee (AJCC) this system is based on description of the primary tumour (T), the status of regional lymph nodes (N), and the presence of distant metastasis (M) [10].

1.1 Aims and Objectives

As breast cancer is one of the leading causes of death in women in developed and developing countries, a need is felt for some simple biochemical investigations like for the early detection of cancer and can be assayed in smaller laboratories located in remote areas. In view of this certain biochemical investigations like LDH, GGT& ALP which are though considered non –specific, carried out in breast cancer patients to establish their diagnostic values in cancer with and without metastasis.

In view of this, the present study was undertaken to evaluate and estimate the certain biochemical investigations like serum Lactate dehydrogenase, Gamma Glutamyl Transpeptidase, Alkaline phosphatise, 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.

2. Materials and Methods

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 40 healthy controls. All of these subjects were taken from surgery department, government general hospital, Kakinada. 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. The consent was obtained both from cases and controls. The observed values were compared with control group for statistical analysis. All data were expressed as mean and ± 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. The study was approved by ethical committee of the institute.

2.1 Inclusion criteria

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

2.2 Exclusion criteria

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

3. Results

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: Levels of different Biochemical parameters in Carcinoma Breast cases and control groups

S. No	Parameter	Controls n=40	Cases (premenopausal) n=30	Cases (post- menopausal) n=30	p value
1	LDH	304.85±47.07	543.22±127.37	748.37±76.42	<0.0001[HS]
2	GGT	24.55±5.92	55.68±14.65	82.83±15.92	<0.0001[HS]
3	ALP	34.15±15.59	114.88±23.84	174.50±23.3	<0.0001[HS]
4	TOTAL PROTEINS	6.917±0.451	7.975±1.034	8.237±1.182	<0.0001[HS]
5	ALBUMIN	4.053±0.422	2.667±0.833	2.665±0.920	<0.0001[HS]
6	GLOBULIN	2.835±0.351	5.310±0.556	5.315±0.526	<0.0602[NS]
7	SGOT	36.20±20.35	66.90±14.03	63.7714.01	<0.0001[HS]
8	SGPT	33.43±18.59	58.70±15.96	59.07±14.95	<0.0001[HS]

Table 2: Pearson correlation coefficient (r value)- Post Menopausal Patients

S. No.	Parameter	r value
1	LDH	+0.1017
2	GGT	-0.2105

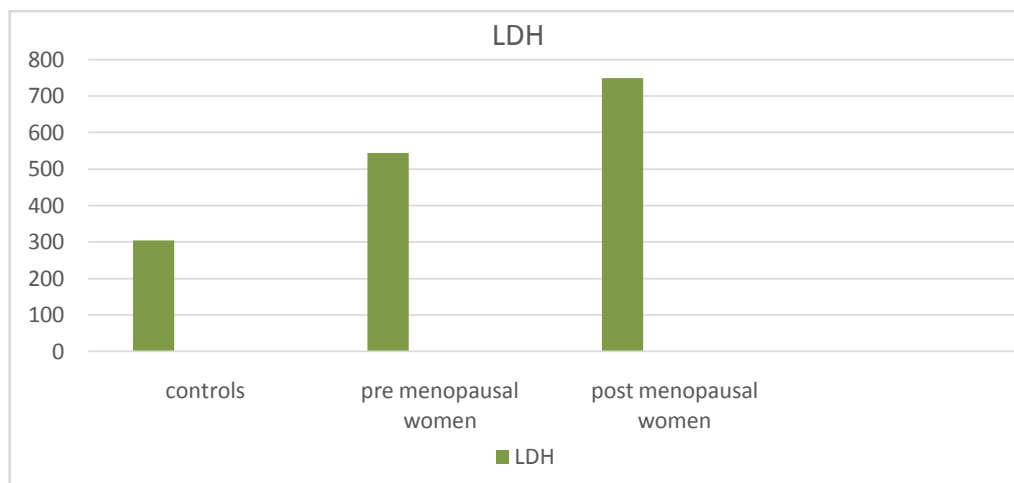Correlation of ALP levels with LDH and GGT levels in post-menopausal patients

Figure 1: Comparison of LDH levels in control, pre-menopausal and post-menopausal women of Ca. Breast cases
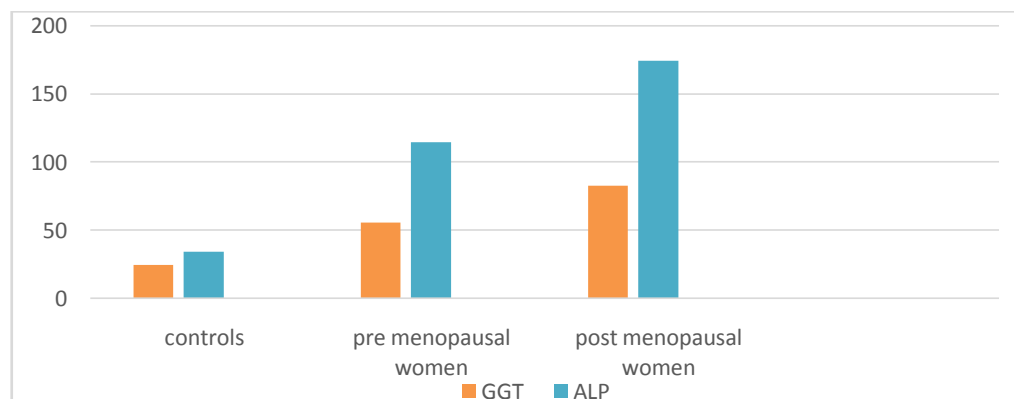

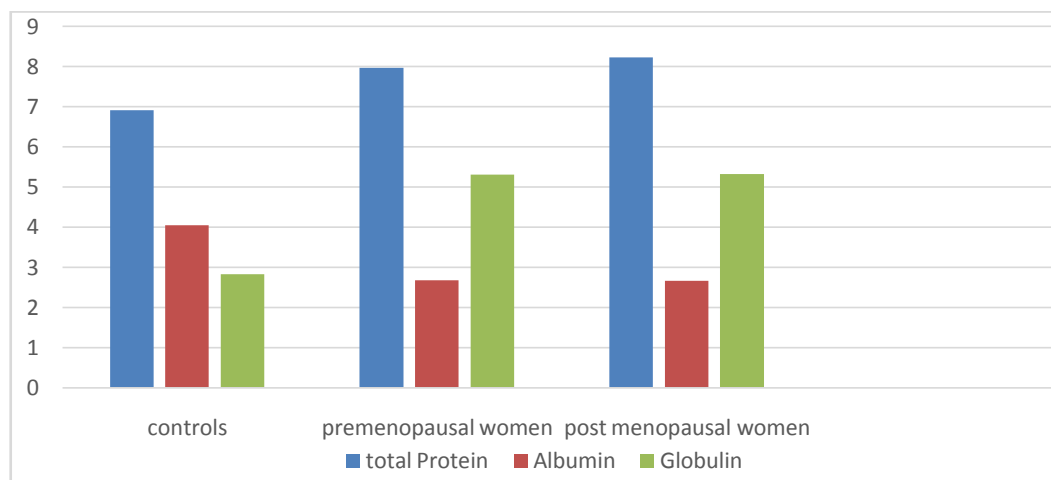**Figure 2: Comparison of GGT and ALP in control, pre-menopausal and post-menopausal women of Ca. Breast cases**

Figure 3: Comparison of total Protein, Albumin and Globulin in control, pre-menopausal and post-menopausal women of Ca. Breast cases

4. Discussion

In present study serum LDH is significantly ($p<0.001$) increased in CA breast patients (mean 543.22 ± 127.37) when compared to controls (mean 304.85 ± 47.07) but further increased in CA breast cases of post-menopausal age group (mean 748 ± 47.07). 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 ($r = + 0.1017$). The present study correlates with Swetha *et al* [11] and Kher *et al*.

Serum GGT is significantly ($p<0.001$) increased in CA breast patients (mean 55.68 ± 14.65) when compared to controls (mean 24.55 ± 5.92) but further increased in CA breast cases of post-menopausal age group (mean 82.84 ± 15.92) It may be due to response of increased reactive oxygen production in the blood[12]. Serum GGT level in CA

breast patients of post-menopausal age group is negatively correlated with ALP (r= - 0.2105). The present study correlates with Seth and Chowdary *et al* [13].

Serum ALP levels (mean 114.88±23.84) is significantly increased (p<0.001) in CA breast patients when compared with controls (mean 34.15±15.59) but further increased in CA breast cases of post-menopausal age group (mean 174±23.3) it may be due to neoplastic metastasis of the liver resulting from localised intra hepatic cholestasis with increased synthesis of enzyme in liver tissue [14]. The present study correlates with Mishra, Waliam, Baumah PK and Coombes Rc and Yes-Tsu N *et al* [15].

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.

5. Conclusion

The present study is restricted to CA breast patients in premenopausal and 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.

The present study shows significant elevation of serum LDH and GGT in total CA breast cases than that controls and in post-menopausal patients LDH and GGT concentrations more markedly increased due to aggressiveness of tumour growth. It is used as a diagnostic and prognostic marker.

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 can be easily assayed, less expensive approached to general population and can detect metastasis also.

References

[1] Mehta S, Mehta A. Breast. In: Ahmed AH, Shrivastava RB, editors. ASI Textbook of Surgery.1st ed. New Delhi: Tata Mc Graw Hill Publishing Company Ltd; 2003. p. 668-99.

[2] Ford D, Easton DF, Stratton M. *et. al*. Genetic heterogeneity and penetrance analysis of the BRCA1 and BRCA2 genes in breast cancer families. *Am J Hum Genet*. 1998; 62:676–89.

[3] Couch FJ, DeShano ML, Blackwood MA. *et al. BRCA1* mutations in women attending clinics that evaluate the risk of breast cancer. *N Engl J Med*. 1997; 336:1409–15.

[4] Truscott BM. Carcinoma of the breast. *Brit J Cancer*. 1947; 1:129. doi: 10.1038/bjc.1947.15.

[5] Collaborative Group on Hormonal Factors in Breast Cancer: Menarche, menopause, and breast cancer risk: individual participant meta-analysis, including 118 964 women with breast cancer from 117 epidemiological studies. *Lancet Oncol* 2012; 13:1141-51.

[6] Brinton LA, Richesson D, Leitzmann MF, Gierach GL, Schatzkin A, Mouw T, *et al*. Menopausal hormone therapy and breast cancer risk in the NIH-AARP. Diet and Health Study Cohort. *Cancer Epidemiol Biomarkers Prev*. 2008; 17:3150-60.

[7] Kumar, Vinay; Abul Abbas (2010). Robbins and Cotran Pathologic Basis of Disease. Philadelphia: Saunders, an imprint of Elsevier inc. p. 1090. ISBN 978-1-4160-3121-5.

[8] Slanger TE, Chang-Claude JC, Obi N, Kropp S, Berger J, Vettorazzi E, *et al*. Menopausal hormone therapy and risk of clinical breast cancer subtypes. *Cancer Epidemiol Biomarkers Prev*. 2009, 18:1188-96.

[9] Li CI Uribe DJ Daling JR: Clinical characteristics of different histological types of breast cancer. *Br J Cancer*, 2005, 93:1046-52.

[10] Das S. The breast. In: A Concised Textbook of Surgery. 5th ed. Kolkata: Dr. S. Das publishers; 2008. p. 691-738

[11] Serum Lactate Dehydrogenase and Lipid Profile in Breast Cancer *IJPBS* 2013; 3(2): 423-43.

[12] Rosalki SB. Gamma-glutamyl transpeptidase. *Adv Clin Chem*. 1975; 17:53–107.

[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 J Med Sci* 2013; 67:123-129.

[14] Kaplan MM. Alkaline phosphatase. *Gastroenterology*. 1972; 62: 452–68.

[15] Mishra Sandhya. Studies of biochemical parameters in breast cancer with and without metastasis. *Indian Journal of Clinical Biochemistry*. January 2004; 19 (1): 71-75.