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SERUM LACTATE DEHYDROGENASE AND LIPID PROFILE IN BREAST CANCER *N.Swetha¹, K.A. Arul Senghor², K. Ramachandran²

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ABSTRACT

Background: Breast cancer is the most common cancer in women. Worldwide, it is estimated that more than 1 million women are diagnosed with breast cancer every year. Cancer of the breast is so widespread that it has become a genuine problem for public health. **Aim:** To analyse serum Lactate Dehydrogenase levels (preoperatively and postoperatively) and investigate the lipid profile in female breast cancer patients. **Materials and Methods:** Fasting blood samples were collected from 20 healthy controls and 20 histopathologically confirmed female breast cancer patients (Premenopausal and Postmenopausal Women) aged 25 to 80 years. Serum Lactate Dehydrogenase (LDH) levels and lipid profile were investigated preoperatively and serum LDH levels were estimated 21 days after the surgery. **Results:** There was a significant increase in preoperative serum LDH levels ($P < 0.001^{**}$) and decrease in postoperative serum LDH levels ($P < 0.001^{**}$) in breast cancer patients as compared to controls. The values of preoperative serum LDH were significantly higher in postmenopausal cases ($P < 0.001^{**}$), LDL-C ($P < 0.001^{**}$), VLDL-C ($P < 0.001^{**}$) and decreased HDL-C ($P < 0.01^{*}$) as compared to controls which were statistically significant. **Conclusion:** The findings of this study suggest that serum LDH might prove to be a biomarker in early detection of the disease and also suggest an immense potential for LDH as a prognostic marker for breast cancer risk.

KEY WORDS

Breast Cancer, Lactate Dehydrogenase, Dyslipidaemia, Prognostic Marker, Preoperative and Postoperative, Premenopausal Women and Postmenopausal women.

INTRODUCTION

Cancer is the second largest killer disease. While cancer accounts for high morbidity and high mortality rate throughout the world, cancer of the breast is common in women in developed countries and more than 40% of all breast cancer cases are found in developing countries ^[1].Cancer starts when a cell begins to divide and grow in an uncontrolled and abnormal way. Overtime these cells cluster to form a tumour. Cancer that is detected early can potentially

be cured when the tumour is small enough to be completely removed surgically ^[2].

Breast cancer is a malignant tumour originating from the breast tissue, most commonly from the inner lining of milk ducts or the lobules that supply the ducts with milk. Breast cancer primarily affects women, accounting for 23% of all female cancers around the globe ^[3]. However, it occasionally affects men; accounting for 0.2% of all cases in men. The female to male ratio of breast cancer prevalence is 100:1^[4].

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Although any portion of the breast, including the axillary tail, may be involved, breast cancer is found most frequently in the upper, outer quadrant ^[5, 6]. The relatively high proportion of carcinomas arising in the upper outer quadrant of the breast is a reflection of the greater amount of breast tissue in this quadrant [7]

Despite the extensive research for many years throughout the world, the etiopathogenesis of cancer still remains obscure. For the early detection of carcinoma of various origins, a number of biochemical markers have been studied to evaluate malignancy.

Enzymes were one of the first groups of tumour markers identified. Under normal conditions, each tissue maintains a steady and consistent enzymatic pattern which is significantly altered in malignancy, because membrane constituents are shed into the surrounding milieu at increased rate when cells replicate more rapidly. The enzymes and protein present in the nucleus, cytoplasm and mitochondria are also released into circulation when cells are destroyed ^[8].

Cancer is a proliferative and invasive disease and the tumour cells respire anaerobically. Firstly, the invading tumour causes severe tissue damage resulting in the release of intracellular enzymes like Lactate Dehydrogenase (LDH) into the blood stream by the injured or dying cells. Secondly, the elevated levels of LDH could be brought about as it is an enzyme essential for anaerobic glycolysis^[9]. In view of this, present study was undertaken to assess LDH in breast cancer.

Dietary fat and obesity affects breast cancer by altering estrogen level. Obesity leads to an overall increase in the active levels of circulating oestrone and oestradiol, which may promote the growth and metastatic potential of breast tumours in obese women^[10].

Malignant proliferation of breast tissue in women has been associated with alterations in serum lipid profile. It has been postulated that changes in the concentration of serum lipids in breast cancer patients could result in increased production of tumour necrosis factor and inhibit adipose lipoprotein lipase activity by the action of insulin ^[11, 12].Elevated lipid levels precede the development of obesity and breast cancer and thus, may have etiological or predictive evidence ^[13].

The principal goal of the study was to analyse serum LDH levels (preoperatively and postoperatively) and investigate the lipid profile in female breast cancer patients.

MATERIALS AND METHODS

Study Population

The study was carried out in 20 histopathologically confirmed female breast cancer patients admitted in the surgical ward at SRM Medical college, hospital and research centre. 20 age and sex matched healthy controls were also included in the study. The control groups were apparently healthy volunteers who were not taking oral contraceptives or any form of hormonal medication. Institutional ethical committee approval was obtained. The participation of the respondents was voluntary and informed consent was signed by each participant. All subjects answered a questionnaire which contained details of age, socioeconomic background, reproductive history and family history of breast or other cancers.

Inclusion Criteria

Premenopausal and postmenopausal women aged 25 to 80 years.

Exclusion Criteria

- Myocardial Infarction
- Haemolytic Anaemia
- Muscular dystrophy
- **Kidney disease**
- Liver disease
- Pancreatitis
- Drugs

Anthropometric Measurement

All the subjects' height and weight were recorded without shoes using standard apparatus. Weight was measured to the nearest 0.1 kg and height was measured to the nearest 0.5 cm. Body Mass Index (BMI) was calculated by dividing weight (kg) by height (m^2) . BMI (kg/m^2) is recognized as the measure of overall obesity. Normal weight was defined as BMI < 25, Overweight as BMI between 25.0 - 29.9 and Obesity as $BMI \ge 30$.

Sample Collection

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Fasting blood samples were collected from healthy controls and female breast cancer patients before surgery and 21 days after surgery. The blood was allowed to clot and serum was separated by centrifugation at 3000 rpm for 10 minutes. All the samples were analysed for LDH and lipid profile on the same day of collection using standard kits in OLYMPUS AU400 Autoanalyzer.

Biochemical Methods

Serum LDH was determined by UV – Kinetic Method. Total cholesterol (TC) and Triglycerides (TG) were assayed by standard enzymatic Procedures. High Density Lipoprotein Cholesterol (HDL-C) was estimated by Precipitation Assay Method. Low Density Lipoprotein Cholesterol (LDL-C) and Very Low Density Lipoprotein Cholesterol (VLDL-C) were calculated using Friedewald's Formula.

Statistical Analysis

The values were expressed as Mean \pm Standard deviation and the findings were analysed by Student "t" test. "P" value less than 0.05 was considered statistically significant. A "P" value with single star (*) represent significant and "P" value with two or three stars (***) represent highly significant.

RESULTS

Serum LDH levels and lipid profile were investigated preoperatively in breast cancer patients and controls. Serum LDH levels were also estimated 21 days after the surgery in breast cancer patients.

Table 1 shows the mean, standard deviation and P values of LDH levels in breast cancer patients and control groups. The preoperative serum LDH activity in breast cancer patients (410.05 ± 44.33) IU/L was significantly increased as compared to controls (245.1 ± 37.06) IU/L; (P<0.001^{**}) and postoperative serum LDH activity in breast cancer patients (298 ± 49.50) IU/L was significantly decreased as compared to preoperative serum LDH activity (410.05 ± 44.33) IU/L; (P < 0.001^{**}). The LDH levels were then estimated in premenopausal and postmenopausal breast cancer patients and compared with the control groups. Preoperative serum LDH was significantly

higher in premenopausal breast cancer patients (372.1 ± 19.85) IU/L as compared to premenopausal controls (219.9 ± 12.03) IU/L; (P<0.0001^{***}). Similarly, Preoperative serum LDH was significantly higher in postmenopausal breast cancer patients (448 ± 23.56) IU/L as compared to postmenopausal controls (271.1 ± 35.38) IU/L; (P < 0.0001^{***}). Serum LDH levels were further compared between premenopausal and postmenopausal breast cancer patients (Before and After Surgery). The values of serum LDH were significantly higher in postmenopausal cases (Before Surgery: 448 ± 23.56) IU/L and (After Surgery: 377.1 ± 19.85) IU/L and (After Surgery: 258.3 ± 32.96) IU/L; (P < 0.001^{**}).

Table 2 contains the mean, standard deviation and P values of BMI and lipid profile in breast cancer patients and controls. BMI was calculated in breast cancer patients and control groups. Breast cancer patients had significantly higher BMI (28 ± 2.24) Kg/m² than the control group (23.56 \pm 1.26) Kg/m²; (P < 0.0001^{***}). Lipid profile was also estimated in breast cancer patients and compared with the control groups. There was a significant increase in serum total cholesterol levels in breast cancer patients (206.8 ± 24.87) mg/dl compared to the controls (181.15 \pm 22.37) mg/dl; (P < 0.001^{**}). There was also a significant increase in serum triglyceride levels in breast cancer patients (151.35 ± 66.58) mg/dl compared to the controls (95.55 ± 30.42) mg/dl;(P < 0.001^{**}). Mean serum HDL – C was significantly decreased in breast cancer patients (35.5 ± 8.22) mg/dl than the control group (42.85 ± 8.08) mg/dl; (P < 0.01^{*}). Mean serum LDL – C was significantly increased in breast cancer patients (140.95 ± 21.57) mg/dl than the control group (119.19 \pm 17.87) mg/dl; (P < 0.001^{**}). Breast cancer patients showed significantly higher VLDL - C levels (30.27 ± 13.32) mg/dl than the control group (19.11 ± 6.08) mg/dl; (P < 0.0001).

Figure 1 shows the mean values obtained for BMI and Biochemical Parameters as bar diagrams.

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Table 1: Mean, Standard Deviation and P Values of LDH Levels in Breast Cancer Patients and Control Groups						
	PARAMETER	GROUPS	Ν	MEAN ± S.D	P – VALUE	
	LDH	Controls	20	245.1 ± 37.06	_ <0.001 ^{**}	
	(IU/L)	Patients(Before surgery)	20	410.05 ± 44.33		
	LDH	Patients(Before surgery)	20	410.05 ± 44.33	<0.001**	
	(IU/L)	Patients(After surgery)	20	298 ± 49.50		
	Premenopausal Women	Controls	10	219.1 ± 12.03		
LDH		Patients(Before surgery)	10	372.1 ± 19.85	- <0.0001	
(IU/L) -	Postmenopausal	Controls	10	271.1 ± 35.38	***	
	Women	Patients(Before surgery)	10	448 ± 23.56	<0.0001	
LDH	Before Surgery	Premenopausal	10	372.1 ± 19.85	<0.001**	
(IU/L)		Postmenopausal	10	448 ± 23.56	_	
(/-/	After Surgery	Premenopausal	10	258.3 ± 32.96	_ <0.001**	
		Postmenopausal	10	337.7 ± 24.17	0.001	

Table 2: Mean, Standard Deviation and P Values of BMI and Lipid Profile in Breast Cancer Patients and Control Groups

PARAMETER	GROUPS	Ν	MEAN ± S.D	P – VALUE
BMI (Kg/m ²) _	Controls	20	23.56 ± 1.26	<0.0001 ^{****}
	Patients	20	28 ± 2.24	
T – CHOL (mg/dl) 🛛 —	Controls	20	181.15 ± 22.37	<0.001 ^{**}
	Patients	20	206.8 ± 24.87	
TGL	Controls	20	95.55 ± 30.42	
(mg/dl)	Patients	20	151.35 ± 66.58	
HDL-C	Controls	20	42.85 ± 8.08	*
(mg/dl)	Patients	20	35.5 ± 8.22	<0.01 [*]
LDL-C	Controls	20	119.19 ± 17.87	<0.001 ^{**}
(mg/dl)	Patients	20	140.95 ± 21.57	- <0.001
VLDL-C	Controls	20	19.11 ± 6.08	
(mg/dl)	Patients	20	30.27 ± 13.32	

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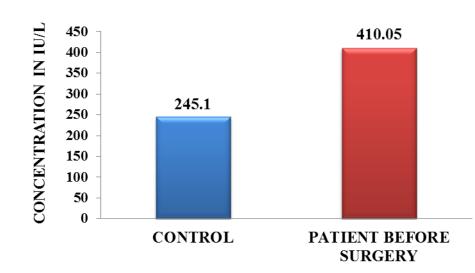


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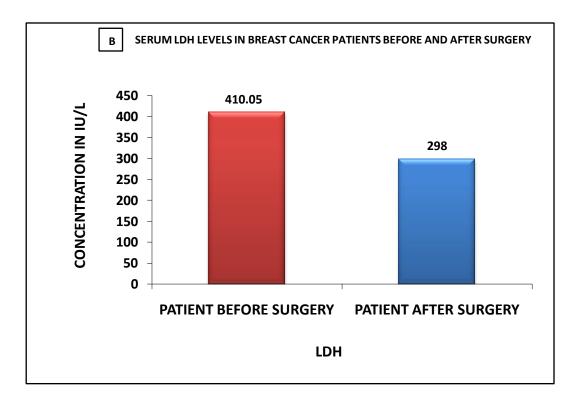
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Figure 1 Comparison of Serum LDH Levels between breast cancer patients and control Group





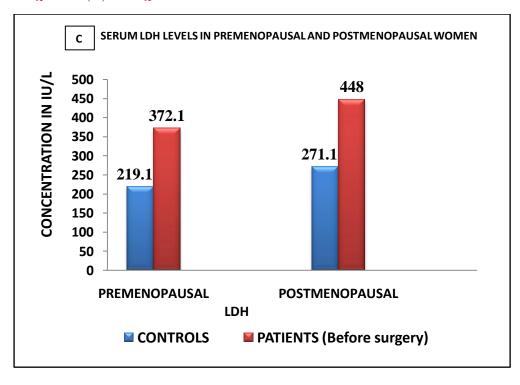


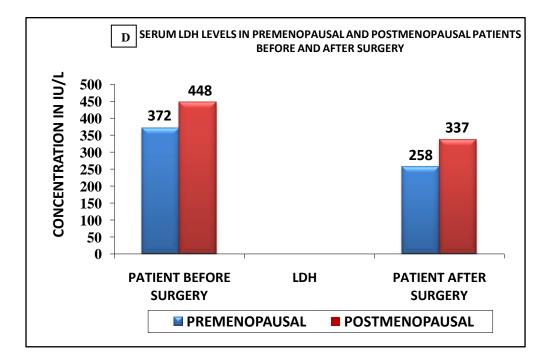


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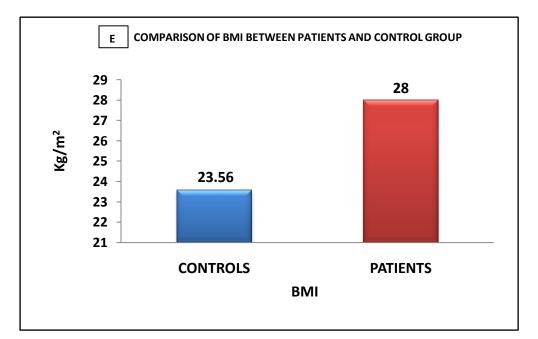
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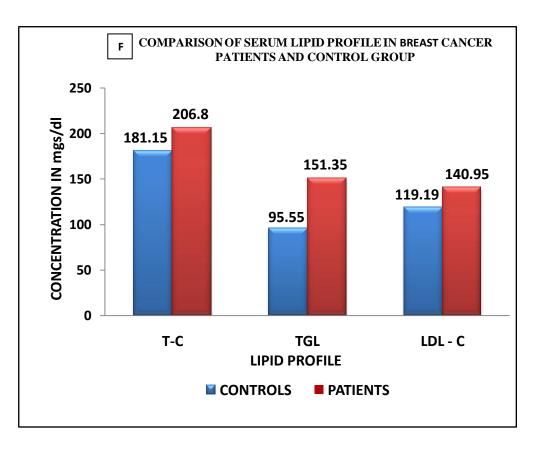




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DISCUSSION

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A total number of 20 patients with confirmed diagnosis of breast cancer and 20 healthy controls were selected to study the levels of Lactate

Dehydrogenase (LDH), BMI, Total cholesterol, Triglycerides, HDL-C, LDL-C and VLDL-C. The patients were followed up and serum LDH levels were also estimated postoperatively. All subjects were divided

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into 2 groups: Premenopausal and Postmenopausal and analysed for LDH; each group consisted of 10 subjects with an age group of 25 to 80 years.

The present study showed significant increase in preoperative serum LDH levels in breast cancer patients as compared to controls. The results were consistent with the study of AnupamaShrinivasan et al., (1999)^[9].

Elevated serum LDH levels in patients with breast cancer have also been estimated by Jagathersan et al., (1962) and Seth et al., (2003) ^[14, 15]. The patients with localized disease showed two and a half-fold increase, whereas five-fold increase was observed in patients with distant metastasis ⁽¹⁵⁾. Thus, serum LDH levels increase enormously once the tumour metastasizes and correlates well with increase in tumour load ^[16].

Malignant conditions are known for demonstrating high levels of LDH ^[9, 17]. Termed as an old enzyme reborn as a cancer marker ^[18], raised levels of LDH are seen in malignancies because of high rate of glycolysis by tumour cells. Release of LDH from dying tumour cells and induction of LDH synthesis in the normal tissues of the host by the tumour ^[19] also contribute to raise LDH levels.

Anupama Shrinivasan et al., (1999) reported significant elevations in both premenopausal and postmenopausal levels of LDH in breast cancer patients as compared to controls. As compared to premenopausal levels, postmenopausal levels of LDH were elevated in breast cancer patients ^[9]. The increase in LDH levels with age and following menopause as seen in controls may be due to the release of the intracellular enzymes from dead cells into circulation since aging is a degenerative process associated with general tissue breakdown and necrosis ^[9].

Kher et al., (1997) correlated post treatment decrease in serum LDH levels with response to therapy^[20]. Similar result of decreased postoperative serum LDH levels was observed in our study.

A study by William K.B.A Owiredu et al., (2009) on serum lipid profile of breast cancer patients showed significant increase in BMI, Total cholesterol, Triglycerides and LDL - C compared to the controls^[10]. Our result was in accordance with the above study.

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Increased levels of circulating lipids and lipoproteins have been associated with breast cancer risk ^[21]. A major link has been established between cell growth and cholesterol biosynthesis. Buchwald (1992) proposed that cholesterol inhibition, either by decreasing cholesterol availability or by decreasing intracellular cholesterol synthesis could inhibit tumour cell growth and possibly prevent carcinogenesis ^[22]. Moyisch et al.,(2000) reported that women with high serum triglyceride levels have an increased breast cancer risk ^[21]. Ray et al.,(2001) suggested that higher levels of total cholesterol and triglycerides may play an important role in carcinogenesis^[23].

William K.B.A Owiredu et al., (2009) reported increased levels of low density lipoprotein cholesterol (LDL-C) in breast cancer patients. The elevated LDL-C concentration, which is more susceptible to oxidation, may result in higher lipid peroxidation in breast cancer patients. This may cause oxidative stress leading to cellular and molecular damage thereby resulting in cell proliferation and malignant conversions^[10].

Elevated or depressed levels of HDL-C in women with breast cancer have been reported. It was found that patients with more advanced breast cancer have significantly lower concentration of HDL-C than do patients with less advanced disease ^[24].

William K.B.A Owiredu et al., (2009) showed that HDL – C remained unchanged $^{[10]}$. But in our study, statistically significant decrease of HDL – C was observed in breast cancer patients as compared to controls.

Epidemiology studies reveal that high density lipoprotein cholesterol (HDL-C) and breast cancer are influenced by variables like dietary fat intake, alcohol consumption, weight, country of residence, pregnancy, endogenous hormones, smoking, exercise and socioeconomic status. HDL-C level has been shown to be higher in subjects with mammographic dysplasia and family history of breast cancer ^[25].

CONCLUSION

The present study showed a significant increase in preoperative serum LDH levels in breast cancer patients as compared to controls. As compared to preoperative serum LDH levels, there was a significant

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decrease in postoperative serum LDH levels. The values of preoperative and postoperative serum LDH were significantly higher in postmenopausal cases as compared to premenopausal cases. It is therefore concluded that serum LDH might prove to be a biomarker in early detection of the disease and also suggest an immense potential for LDH as a prognostic marker for breast cancer.

Breast cancer patients had high BMI with increased total cholesterol, triglycerides, LDL - C, VLDL - C and decreased HDL - C as compared to the controls which was statistically significant. Thus, higher BMI is associated with breast cancer risk. It can also be stated that higher levels of total cholesterol and LDL -C may play a significant role in carcinogenesis. The findings of this study confirm the association between BMI, dyslipidemia and increased breast cancer risk.

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