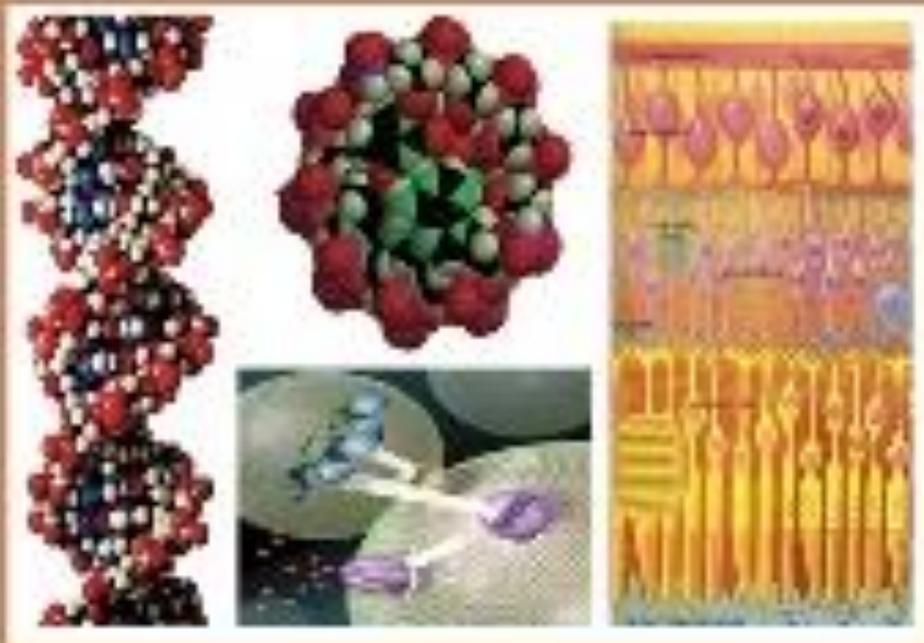




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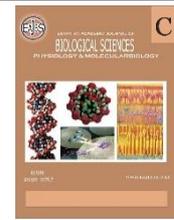
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Evaluate the Levels of Lysophosphatidic Acid and Lipid Profile in Patients with Breast Cancer

Reham A. Khaled¹ ; Rafah R. H. Al-Samarrai^{2*} and Ahmed Z. Abdel Hamid

¹Department of Pathological Analysis, College of Applied Science, University of Samarra, Salahaddin, Iraq.

²Department of Applied Chemistry, College of Applied Science, University of Samarra, Salahaddin, Iraq.

³Medical oncology specialist, Oncology Teaching Hospital Baghdad Medical City, Medical Oncology Department, Oncology Teaching Hospital Baghdad, Baghdad, Iraq.

*E-mail: dr.rafeh_alsamarrai@uosamarra.edu.iq

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ABSTRACT

The current study aims to evaluate the levels of lysophosphatidic acid-LPA and lipid profile in sera of women with breast cancer-BC. Ninety serum samples were taken from women; 30 samples were taken from healthy women (control group-C) without a history of BC, and 60 samples were divided into two groups: 30 untreated BC patients as first group-G1, and 30 post-treatment as the second group-G2.

The study includes the determination of the level of serum LPA, total cholesterol-TC, triglycerides-TG, high-density lipoprotein-HDL, low-density lipoprotein-LDL and very low-density lipoprotein-VLDL.

The results indicate that the value of body mass index-BMI was significantly higher in G1 as compared with G2 and the control group. The level of LPA and HDL was significantly elevated in the patients' group, while the levels of serum TC, TG, LDL, VLDL and TC/HDL ratio were significantly decreased in the patients' groups(G1 and G2) as compared with C.

From the results of the current study, we can conclude that LPA plays an important role in the development of BC in new diagnostic cases or after treatment, while the correlation between lipids and breast cancer is obscure and needs more studies.

INTRODUCTION

Breast cancer-BC is one of the most malignancy diseases prevalent in women. However, most types of BC are benign and treatable by surgery (Hatsell, S., *et al.*, 2003) and others are metastatic cancer that can transport to other organs such as lungs, bones, liver and brain which is mostly the reason for its incurability (DeSantis, C. E., *et al.*, 2016). Current drugs that are used in the treatment of the disease delay the progression of the tumour, but in most cases, repetition of the tumour is inevitable, causing increasing the risk of mortality among patients (Hatsell, S., *et al.*, 2003). The lack of knowledge or proper awareness of breast cancer and delayed diagnosis are the main causes of the high prevalence and deaths of the disease (da Costa Vieira, R. A., *et al.*, 2017 and Tfayli, A., *et al.*, 2010).

The main significant risk factors for the development of BC are genetic factors, marriage in delayed age, lifestyle, environmental factors, hormonal replacement therapy, late first child and obesity (Parkin, D. M., and Fernández, L. M. 2006 ; Lehmann, B. D., *et al.*, 2015 and Sánchez-Jiménez, F., *et al.*, 2019), while, Garcia-Estevez, L., and Moreno-Bueno, G. (2019), indicate that obesity and cholesterol affect the clinical outcomes of BC patients, so physicians are recommending patients to lose body weight and change the lifestyle for obese patients with BC. Obesity is strongly correlated with dyslipidemia, Many studies evaluate the correlation between dyslipidemia and BC, but the results are conflicting. Owiredu, *et al.*, (2009), confirm this correlation between dyslipidemia and increased BC risk, while Abdelsalam *et al.* (2012) indicate that the development of BC may be considered as one factor for lipid profile level variation. So, the present study aimed to evaluate the levels of lipid profile and lysophosphatidic acid-LPA in sera of women with BC.

MATERIALS AND METHODS

Study Design:

Serum samples were obtained from 90 women, 30 samples were collected from healthy women without a history of BC as control group-C, and 60 samples for patients with BC were divided into two groups. The first group-G1 Includes 30 samples from untreated women with BC and the second group-G2 includes 30 samples from post-treatment women with chemotherapy.

The patients' samples were collected

from the Oncology Teaching Hospital-Baghdad in the period between 1/11/2022-15/1/2023.

Methods:

The study includes the determination of the concentration of serum lysophosphatidic acid, using enzyme-linked immunosorbent assay-ELISA and also the determination of the serum concentration of total cholesterol-TC, triglycerides-TG, high-density lipoprotein-HDL using enzymatic colourimetric kits(Allain, C.C., *et al.*, 1974 ; Richmond, W.1992 and Burstein, M., *et al.*, 1980.), while the concentration of serum low-density lipoprotein-LDL and very low-density lipoprotein-VLDL were calculated by Friedewald's equation (Friedewald, W.T., *et al.*, 1972).

The obtained data were analyzed using Duncan's Multiple Range tests by Statistical Packages for Social Science Software-SPSS, at the value of $P \leq 0.05$ is considered significant.

RESULTS AND DISCUSSION

The results of the current study are summarized in Table 1. The table showed that the age was matched between the patient groups and control groups, the value of body mass index-BMI was significantly higher in G1 as compared with G2 and control group. The level of LPA and HDL was significantly elevated in the patients' group as compared with C, while the levels of serum TC, TG, LDL, VLDL and TC/HDL ratio were significantly decreased in the patients' groups(G1 and G2) as compared with C.

Table 1: The mean \pm Standard deviation for parameters under investigation

Parameters	Control group	First group	Second group
Age (year)	45.666 \pm 7.023a	48.966 \pm 11.189a	47.900 \pm 9.721a
BMI(Kg/m ²)	30.841 \pm 5.050b	32.093 \pm 6.934a	29.019 \pm 4.91b
LPA(ng/ml)	24.446 \pm 2.772c	42.149 \pm 10.998b	45.920 \pm 4.825a
TC(mg/dl)	215.086 \pm 12.444a	196.199 \pm 11.180b	169.716 \pm 12.657c
TG(mg/dl)	224.334 \pm 14.121a	205.389 \pm 14.964b	177.373 \pm 22.059c
HDL(mg/dl)	29.552 \pm 3.527c	34.395 \pm 2.576b	40.667 \pm 3.593a
LDL(mg/dl)	140.671 \pm 13.226a	120.731 \pm 10.830b	93.578 \pm 12.062c
VLDL(mg/dl)	44.862 \pm 2.825a	41.073 \pm 2.993b	35.471 \pm 4.412c
TC/HDL	7.43 \pm 1.428a	5.756 \pm 0.788b	4.224 \pm 0.696c

Lysophosphatidic acid is a simple bioactive phospholipid molecule, soluble in water, composed of a glycerol backbone, free phosphate group with a single fatty acyl chain (Pagès, C., *et al.*, 2001 and Mills, G. B., & Moolenaar, W. H. 2003). It can contribute with its G protein-coupled receptors-GPCR in the development of different types of cancers, such as colorectal cancer (Yang, M., *et al.*, 2005), hepatocellular carcinoma (Kaffe, E., *et al.*, 2019), pancreatic cancer (Lv, G. M., *et al.*, 2011), and lung and breast cancer (Ray, R., *et al.*, 2020).

LPA is a growth factor that plays an important role in BC metastasis to bone due to its ability to promote survival, migration and proliferation for the cells by acting on its receptor (GPCR), which contributes to both cancer progression and metastasis (Nam, J. S., *et al.*, 2018 and Balijepalli, P., *et al.*, 2021). Otherwise, the increase in the level of LPA after undergoing chemotherapy may be due to its release to the bloodstream from the damaged cells (including the normal and cancer cells) affected by the chemotherapy or also may be produced from the remaining cancer cells not affected by the treatment which become more aggressive.

The results of this study about the lipid profile indicate a significant decrease in the level of TC, TG, LDL and VLDL with a significant elevated in the level of HDL in sera of patients groups (G1 and G2). This finding disagrees with the findings of other studies, which demonstrate that a higher level of VLDL and a low level of HDL significantly correlated with BC (Chang, S. J., *et al.*, 2007), while the study of Hasija, K., and Bagga, H. K. (2005), indicate that the level of VLDL and HDL has not significantly changed in the sera of women with BC, but the ratio between TC/HDL is significantly elevated. The results of the lipid profile agreed with the finding of Shah, F. D., *et al.*, (2008). which showed that the levels of TC, TG, and VLDL were significantly lower after treatment.

Conclusion:

Lysophosphatidic acid plays an

important role in the development of breast cancer, in new diagnostic cases or after treatment, while the correlation between lipids and breast cancer is obscure and needs more studies.

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