ALTERATION IN SERUM LIPID PROFILE LEVELS IN IRAQI WOMEN WITH BREAST CANCER BEFORE AND AFTER CHEMOTHERAPY

RANA HAZIM HAMOODE[1], MOHAMMED QAIS AL-ANI[2]*, FAREED ARRAK TURKEY[3]

[1]Department of Basic Sciences, University of Anbar-College of Dentistry, Ramadi, Iraq. [2]Department of Biology, University of Anbar-College of Science, Ramadi, Iraq. [3]Department of Surgery, Baghdad Teaching Hospital, Medical City, Ministry of Health, Iraq.
Email: drmohammedqais1975@gmail.com

ABSTRACT

Objective: Investigating the role of alterations in lipid profile in Iraqi women with breast cancer before and after chemotherapy.

Methods: A total number of 100 patients aged 25–47 years were enrolled in this study, including 35 breast cancer treatment patients, 30 treatment patients, and 10 and 25 healthy women benefactor. All samples were collected from August 2016 to February 2017 from Oncology Hospital/Medical city in Baghdad; however, control group samples were collected from outside the hospital. Serum total cholesterol, serum triglyceride, and serum high-density lipoprotein cholesterol (HDL-C) were measured by spectrophotometer using a kit provided by Linear Chemicals.

Results: The results show a highly significant increment (p<0.01) in lipid profile in breast cancer, especially in diagnosis group as compared with other groups.

Conclusion: The alteration in cholesterol, triglyceride, HDL-C, and very low-density lipoprotein is highly connected with breast cancer in Iraqi women, progression of disease and treatment effect.

Keyword: Breast cancer, Lipid profile, Triglyceride, High-density lipoprotein, Chemotherapy, Iraqi women.

INTRODUCTION

Breast cancer is the most common type of cancer in women; about 80–90% of all breast cancer infiltrating ductal carcinoma [1,2]. Current treatment of breast cancer is based on combination therapy using radiotherapy, chemotherapy and cytotoxic molecules and antibodies targeting cancer cells [3]. It is responsible for the death of millions of women worldwide every year.

Malignancy of the breast is one of the most common causes of death in women aged between 40 and 44 years [4]. The precise cause of breast cancer is unknown; however, the female sex hormone estrogen [5] is reported to be the main cause since it promotes the cellular growth in the tissues of the breast and reproductive organ [6]. The risk of breast cancer increases with a high-fat diet [7], obesity [8], use of contraceptives [9], lack or short duration of breastfeeding, and family history of breast cancer [10]. Breast cancer occurs mainly in females [11]. It is considered to be the most invasive cancer in the world. It represents 22.9% of invasive cancers in women nearly 18.2% of cancer deaths worldwide including females and males are caused by breast cancer. High rate of breast cancer is reported in developed nations compared to less rate developing ones [4]. Furthermore, changes in lipid profile have been associated with cancer because lipids play a key role in maintenance of cell integrity; malignant proliferation of breast tissue in women has been associated with changes in plasma lipid and lipoprotein levels [12]; it has been postulated that changes in concentration of serum lipid in breast cancer patients could lead to increase production of tumor necrosis factor [13,14]. Dietary lipids are found to have an association of breast cancer recurrence and survival of cancerous cells. Lipids as the part of cell membranes signal molecules and energy substrates play a key role in breast cancer. Previous studies reported a correlation between fat and breast cancer suggesting that dietary fat plays an important role in the incidence of breast cancer, in an animal model [15].

Dietary fat is directly associated with breast cancer as the fat is composed of fatty acids which have distinctive biophysical and chemical properties that can influence on breast cancer disease and normal health [16]. Lipoproteins are the distributors of both endogenous and exogenous lipids across the tissues. It is, therefore, possible that lipoproteins can play a fundamental role in the progression of cancer through lipids supply to malignant cells and tumors. The level of plasma lipids reflects the dietary lipid intake in individuals. There are several reports of increased plasma lipid levels such as triglycerides, total cholesterol, and low-density lipoproteins cholesterol (LDL-C) in breast cancer patients [14].

METHODS

This study was conducted from August 2016 to February 2017 on a total number of 100 subjects including 35 breast cancer patients (they are still not receiving adjuvant treatment), 30 treated patients, 10 worker group (working in the room, they do blending and preparer of chemotherapy for patients in the hospital), and 25 healthy women benefactor. All samples were collected from Oncology Hospital/Medical city in Baghdad; however, control group samples were collected from outside the hospital.

Collected blood samples 4 mL were taken from each women patients and control group, placed into Gel tubes, left a round 15 min at room temperature and it is centrifuged at ×2000 g for 10 min to get the serum, to be used while in measurement of each of lipid profile.

Determination of serum lipid profile
Serum Lipid Profile was measured by Spectrophotometer using a kit provided by Linear Chemicals S.L Spain. (http://www.linear.es), or colorimeter capable of measuring absorbance at 500 ± 10 nm.

Table 1: The mean serum lipid profile in different women with breast cancer and control

Parameter	Mean±SE of lipid profile				
	Cholesterol mg/dl	Triglyceride mg/dl	HDL mg//dl	VLDL mg/dl	LDL mg/dl
Diagnosis group N=35	218.57±5.7	263.45±22.62	54.80±1.58	52.49±4.5	111.29±7.49
Treatment group	194.03±7.6	166.97±14.14	52.47±2.35	33.40±2.8	108.17±5.65
Worker groupN=10	158.40±6.6	173.30±37.61	51.90±3.58	34.70±7.5	71.80±8.31
Control group=25	153.68±2.9	121.04±1.63B	34.60±0.87B	24.36±0.3	94.72±3.02
LSD value	20.230**	61.468**	6.249**	12.307**	20.979**
p-value	0.0001	0.0001	0.0001	0.0001	0.0061

*(p<0.05), **(p<0.01), NS: Non-significant, SE: Standard error, LSD: Least significant difference, P: Probability value of significance, Means having with the different letters in same column differed significantly, HDL: High-density lipoprotein, VLDL: Very low-density lipoproteins

RESULTS

Serum lipid profile level indices in studied groups

Table 1 summarizes the mean ± standard error of lipid profile levels. There was a highly significant increment (p<0.01) in lipid profile (cholesterol, triglyceride, high-density lipoprotein cholesterol [HDL-C], very LDL [VLDL], and LDL) level in breast cancer, especially in diagnosis group as compared with other studied groups.

DISCUSSION

In the present study, lipid profile was determined in Iraqi women with breast carcinoma, pretreatment (before any treatment), after chemotherapy three dose and with history family. Other studies have been published, also focused on determining lipid profile in breast carcinoma women. In the present study, a significant difference in total cholesterol, LDL-C, and decrement HDL-C levels was found between cases and control [17,18]. We found that total cholesterol and triglyceride fraction is significantly associated with breast cancer progression and may actually be useful in the identification and medical follow-up of high-risk groups, total cholesterol, and triglyceride highly levels at diagnosis, therefore, may germinate as a prognostic factor in breast cancer patients and in most of those who developed disease progression. These findings were consistent with that of other studies [18].

Regarding that proliferating cancer cells have an incremented demanding of cholesterol and intermediates of cholesterol biosynthesis pathway, the upregulation of cholesterol biosynthesis and decreased cellular efflux are expected. In cancer cells, cholesterol synthesis has been shown to be increment, due to availability of precursors or to raised transcription and this may have contributed to breast cancer carcinogenesis [19]. Hydroxy-3-methyl-glutaryl-coA reductase 3 inhibition by statins decreases *in vitro* cell proliferation, attesting that cholesterol biosynthesis should be important to tumor growth. Moreover, elevated cholesterol content is characteristic of breast tumors [20].

In the present study, increment triglyceride in the pretreatment patients group compared to the after treatment and control group shown in Table 1, this defect may demonstrate that triglyceride plays central roles in the development of breast carcinoma. After treatment, we also notice Rias of triglyceride compared to control group; this increase might be due to the intake of tamoxifen [20]. It is known that tamoxifen is prescribed for patients with breast cancer as a chemotherapy treatment. However, it was reported that such a drug has a side effect and alters the level of cholesterol and triglyceride [20].

The studies reveal that the increment level of HDL-C highly than the after treatment compared to control group. The increment was attributed to the effect of high level of estrogen, progesterone hormones, after taking the drugs is likely to cause raise in its level [21], the increment in HDL might be due to the influence of tamoxifen, which is given as a treatment to decrement risk of breast cancer and but caused raise in HDL level substantially [22]. These studies were found to be consistent with the study by other investigators [23].

This study also found that high level of LDL was not significant in their pretreatment and after treatment compared with control group, high levels of LDL were associated with increased breast cancer risk, which agree with previous study done by Owiredu *et al.* [24], Abdullah *et al* [25], and disagree with studies by Sung *et al.* [26].

The raised serum LDL is marked susceptible to oxidation. This may cause oxidative stress leading to cellular and molecular damage, thereby resulting in cell proliferation and malignant conversion.

Concerning VLDL, the present study found that there was no association with breast cancer risk, and these agree with finding of [27,28].

Difference in results obtained in our study and previous research in breast cancer and alteration of lipid profile levels in patients may be due to the progression of the cancer and the side effect of chemotherapy, in addition to environmental, behavioral, and genetic differences [29].

CONCLUSION

This study concludes that there is highly significant connection between raise of serum lipid profile and risk of breast cancer in Iraqi women. In addition, the miscellaneous nature of the complex metabolic pathways in which cholesterol and triglyceride participate allows this lipid to play multiple roles in cancer progression. Further, research on mechanisms for the effects of cholesterol, triglyceride, HDL-C, VLDL, and LDL after taken chemotherapy and its relationship to cancer, which can lead to the discovery of new ways of therapeutic intervention, particularly in controlling progression to late-stage disease.

REFERENCES

1. Siegel RL, Miller KD, Jemal A. Cancer statistics 2015. CA Cancer J Clin 2015;65:5-29.
2. Jagsi R. Progress and controversies: Radiation therapy for invasive breast cancer. CA Cancer J Clin 2014;64:135-52.
3. Paley PJ. Screening for the major malignancies affecting women: Current guidelines. Am J Obstet Gynecol 2001;184:1021-30.
4. Ritu Y, Rajeev S, Preeti C. ER, PR, Her2/Neustatus and Relation to clinic pathological factors in breast carcinoma. Int J Pharm Pharm Sci 2015;8:287-90.
5. Cicatiello L, Mutarelli M, Grober OM, Paris O, Ferraro L, Ravo M, *et al.* Estrogen receptor alpha controls a gene network in luminal-like breast cancer cells comprising multiple transcription factors and microRNAs. Am J Pathol 2010;176:2113-30.
6. Kumar K, Sachdanandam P, Arivazhagan R. Studies on the changes in plasma lipids and lipoproteins in patients with benign and malignant breast cancer. Biochem Int 1991;23:581-9.
7. Schreier LE, Berg GA, Basilio FM, Lopez GI, Etkin AE, Wikinski RL, *et al.* Lipoprotein alterations, abdominal fat distribution and breast cancer. Biochem Mol Biol Int 1999;47:681-90.
8. Narod SA, Dubé MP, Klijn J, Lubinski J, Lynch HT, Ghadirian P, *et al.* Oral contraceptives and the risk of breast cancer in BRCA1 and BRCA2 mutation carriers. J Natl Cancer Inst 2002;94:1773-9.
9. Lalloo F, Varley J, Ellis D, Moran A, O'Dair L, Pharoah P, *et al.* Prediction of pathogenic mutations in patients with early-onset breast cancer by family history. Lancet 2003;361:1101-2.
10. Adam A, Elgadir AM, Salama M. Anti-breast cancer from various

natural sources, review. Int J Pharm Pharm Sci 2015;7:44-7.

11. Samson B, Jayabharathi B. Lived in experience of women with breast cancer. Asian J Pharm Clin Res 2016;9:80-4.

12. Wernberg JA, Yap J, Murekeyisoni C, Mashtare T, Wilding GE, Kulkarni SA, *et al.* Multiple primary tumors in men with breast cancer diagnoses: A SEER database review. J Surg Oncol 2009;99:16-9.

13. Lane DM, Boatman KK, McCarty WJ. Serum lipid and lipoproteins in women with breast masses breast cancer. Res Treat 1995;34:161-9.

14. Knapp ML, AL Sheibani S, Richer P. Galteration of serum lipids in breast cancer. Effect of disease activity treatment and hormonal factor. Clin Chem 1991;37:2093-101.

15. Ahiuwalia S, Shah N. Animal venom for treating breast cancer. Int J Pharm Pharm Sci 2014;6:24-30.

16. Wynder EL, Cohen LA, Muscat JE, Winters B, Dwyer JT, Blackburn G, *et al.* Breast cancer: Weighing the evidence for a promoting role of dietary fat. J Natl Cancer Inst 1997;89:766-75.

17. Ray G, Husain SA. Role of lipids, lipoproteins and vitamins in women with breast cancer. Clin Biochem 2001;34:71-6.

18. Strohmaier S, Edlinger M, Manjer J, Stocks T, Bjørge T, Borena W, *et al.* Total serum cholesterol and cancer incidence in the Metabolic syndrome and Cancer Project (Me-Can). PloS One 2013;8:e54242.

19. Hussain DA, Ahmed S, Hoque M, Rabbi SM, Masood S, Shafi T, *et al.* Biochemical factors associated with breast cancer in Bangladeshi Women. Bangladesh J Med Biochem 2013;6:58-62.

20. Morimoto LM, White E, Chen Z, Chlebowski RT, Hays J, Kuller L, *et al.* Obesity, body size, and risk of postmenopausal breast cancer: The women's health initiative (United states). Cancer Causes Control 2002;13:741-51.

21. King MC, Wieand S, Hale K, Lee M. Tamoxifen and breast cancer incidence among women with inherited mutations in BRCA1 and BRCA2. JAMA 2002;12:58-62.

22. Shyamala G, Schneider W, Guiot MC. Estrogen dependent regulation of estrogen-receptor gene expression in normal mammary gland and its relationship to estrogenic sensitivity. Br Med J 1992;2:121-8.

23. Ridker PM, Stampfer MJ, Hennekens CH. Plasma concentration of lipoprotein and the risk factors of breast cancer JAMA 1995;5:31-5.

24. Liqaa OA. Study effect of breast cancer on some hematological and biochemical parameters in babylon province, Iraq. J Pharm Bioallied Sci 2014;9:20-4.

25. Owiredu WK, Donkor S, Addai BW, Amidu N. Serum lipid profile of breast cancer patients. Pak J Biol Sci 2009;12:332-8.

26. Abdullah EA, Ahmed FA, Adam ZE, Ibrahim OB, Morsi AN. The association between lipid profile and breast cancer in Sudanese women. Sch J Appl Med Sci 2015;3:1992-2000.

27. Sung J, Ha M, Song YM. Serum total cholesterol and the risk of breast cancer in postmenopausal Korean women. Cancer Causes Control 2009;20:1055-60.

28. Chang SJ, Hou MF, Tsai SM, Wu SH, Ann Hou L, Ma H, *et al.* The association between lipid profiles and breast cancer among Taiwanese women. Clin Chem Lab Med 2007;45:1219-23.

29. Peela JR, Jarari AM, El Saiety SO, El BusaifiS, El Awamy H. The relationship between serum Lipids and Breast cancer in Libya. Clin Chem 2010;56 (Supl-6)..