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Research Article

Evaluation of Serum Lipid Profile after Treatment with Various Chemotherapeutic Scheduals in Iraqi Breast Cancer Patients

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ABSTRACT

Breast carcinoma is the most widespread neoplasm worldwide. It ranks first in causing death in Iraqi women. This study aimed to examine the influence of taxane, cyclophosphamide and doxorubicin on the lipid profile in Iraqi patients with breast cancer. This research was acheived in the Departement of Clinical Sciences , Baghdad College of Medical Sciences, and at the main Clinic of Oncology in Baghdad, Iraq, within the interval of June 2019 till November 2019. It included fifty six patients with the regular menstrual cycle (25-45 years) categorized into 3 groups: Group one GI: twenty nine patients with primary breast cancer (before begining chemotherapy), group two, GII: the same twenty nine patients of GI whose completed four circles of anthracyclines (course I) and group three, GIII: who included other twenty seven patients whose acheived both courses; (course one) and four circles of taxanes (course II). Serum total cholesterol (Tch), high- density lipoprotein (HDL), low- density lipoprotein (LDL) and triglycerides (TG) were analyzed using colorimetry based techniques. The outcomes of the current study appears that the (mean ± SEM) of the Tch was reduced significantly ($p<0.05$) within GIII in comparsion to GI and highly significantly ($p<0.01$) in comparsion to GII. While, the serum HDL level was significantly ($p<0.05$) decreased in GIII in comparsion to GI. Concerning the serum LDL level, it was raised significantly ($p<0.05$) in GII in comparsion to both GI and GIII. While; the serum TG level shows no significant difference between all groups. In conclusion, Iraqi women with breast cancer had an abnormal state of dyslipidemia that become worsened after chemotherapy.

Keywords: Chemotherapy, Breast cancer , cholesterol, LDL, HDL, TG.

INTRODUCTION

Carcinoma of the breast is a widely common neoplasm among women around the industrialized world. It was increased steadily over the past 40 years. It is considered the second cause of mortality among women ages 20-59 (Jemal et al, 2003) . In Iraq, it is the first in ranking among cancers (Arkan, 2016). The cause of the disease is unknown, but it could be hormonal, environmental, genetic, radiation, oncogenic viruses and dietary factors (Owiredu et al, 2009). Many factors affect the relation of lipid changes with breast cancer and this relationship is still a subject of controversy. Lipids are the major component of membrane´s integrity in the biological cells, it plays roles in cell growth and development; both for the normal and malignant ones. Lipids are richly present in the mammary tissue. Some studies had found that changes in plasma lipids and lipoproteins are associated with the proliferation of malignant cells in the breast tissue. Recently, they had studied the role of both the endogenous and dietary lipids in the etiology and prognosis of cancer (Seema, 2015). The unbalanced lipid parameters including raised TCh, LDL and TG along with decreased HDL could be a jeopardy for cardiovascular diseases (Xin et al, 2018).

SUBJECTS AND TECHNIQUES

The current study was carried out at the Clinical Chemistry Departement of Baghdad College of Medical sciences and in the Main Oncology Clinic, Baghdad, Iraq, through the interval of June 2019 to November 2019. It comprised of fifty six Iraqi patients diagnosed by Consultant Clinical Oncologist to have had primary carcinoma of the breast; their ages range was 25-45 years. The included women were categorised into groups in respect to their condition of treatment: Group 1 [GI] involved twenty nine patients with primary breast cancer who never subjected to chemotherapy treatment, group 2 [GII] governed the same twenty nine patients of GI, but after ending the 1st course of treatment [4 circles of anthracyclines including Doxorubicin 60mg/m^2 and Cyclophosphamide 600mg/m^2], and group 3 [GIII] that included another twenty seven patients whose finished a complete chemotherapeutic regimen [(course I) and 4 circles of Taxane including (Docetaxel) 100mg/m^2; (course II)]. Exceptions involved pregnancy, smoking, alcohol, anti-inflammatory drugs and patients with hypertension, diabetes and other chronic illness. Formal accptance was gathered from each woman. The authors obtained the moral agreement from the Scientific board of the Clinical Chemistry Departement of Baghdad College of Medical Sciences. New colorimetry based techniques were used to measure serum Tch, LDL HDL and TG. Five milliliters of blood was withdrawn from each involved patient, moved out into an ordinary tube, let to clot and the serum was separated directly by centrifugation at 2500–3000 rpm for 10 min. Investigations included serum measurements of cholesterol, HDL, LDL and TG by colorimetric methods. All the chemical kits were supplied from Germany. The statistical analysis including analysis of variance and t-test were applied to calculate the significant differences among the studied groups . Correlation among different studied parameters in each studied group was inspected by linear regression test [r] and the r-value significance was calculated by the correlated t-test. When the P-value was less than 0.05 , it was treated as significant.

RESULTS

The demographic data in table 1 depicts that there was no significant difference in mean values of age between GI (38.79 ± 0.91 years) and GIII (39.59 ± 0.95 years). Similarly, mean values of BMI were comparable and did not differ significantly between GI (30.04 ± 0.94 Kg/m^2) and GIII (31.78 ± 1.24 Kg/m^2).

Table 1: Age and Body Mass Index values in GI and GIII

Parameters	GI (n=29)	GIII (n=27)
Age ^{NS} **(years)**	38.79 ± 0.91	39.59 ± 0.95
BMI^{NS} **(kg/m2)**	30.04 ± 0.94	31.78 ± 1.24

All values were expressed as Mean (±SEM). BMI: body mass index; ANOVA test revealed a non- significant difference between groups (NS)

Table 2 reveals the Mean (±SEM) of the measured lipid parameters. It shows that the serum levels of cholesterol were found to be non significantly increased in women who finished the first course of chemotherapy treatment [GII; 208.37 ± 8.62 mg /dl] when compared to their levels before treatment [GI; 193.75± 6.83 mg /dl]. However, it was significantly decreased in women who had finished complete courses of treatment [GIII; 168.30 ± 8.14 mg /dl] when compared to that of GI and GII; [$P < 0.05$] and [$p < 0.01$] respectively. Similarly, serum LDL was significantly elevated in GII [125.89 ± 8.88 mg/dl] in comparison with each of GI [104.24 ± 7.17 mg /dl] and GIII [91.02 ± 7.64 mg/dl]; [$P < 0.05$] . Regarding serum HDL level, it was decreased in post-treatment groups compared to that before treatment, but with an only significant [$p < 0.05$] difference between GIII and GI. While, there was no significant level in the serum TG among all groups.

Table 2: Values of Serum Cholesterol, HDL , LDL and TG in GI, GII and GIII

Parameter	GI (n=29)	GII (n=29)	GIII (n=27)
Cholesterol mg/dl	193.75± 6.83●	208.37 ± 8.62●	168.30 ± 8.14
LDL mg/dl	104.24 ± 7.17	125.89 ± 8.88●●	91.02 ± 7.64
HDL mg/dl	58.60 ± 2.34	52.94 ± 3.71	47.61 ± 1.47●●●
TG mg/dl ^{NS}	154.37 ± 7.80	147.68 ± 7.16	148.33 ± 9.55

LDL: low density lipoprotein, HDL: high density lipoprotein, TG: triglycerides. Data are shown as mean (±SEM). ANOVA and t-test revealed
● significant increase of total cholesterol in G1 and G2 than G3; [$p < 0.05$] and [$p <0.01$] respectively,
●●significant increase of LDL in G2 than G1 and G3 [$p<0.05$] ,
●●●significant decrease of HDL in G3 in comparsion to G1 [$p < 0.05$], NS: non- significant differences.

The present study showed that women of G1 exhibited significant direct relationship between serum total cholesterol levels and LDL in G1($r=0.95$, $p<0.01$). Also, serum TG and HDL levels showed significant inverse correlation ($r= -0.394$, $p< 0.05$). Furthermore, a significant but negative correlation was noticed between serum LDL and HDL levels ($r= -0.44$, $p<0.05$) in G1. With respect to G2; an inverse significant relationship can be seen between age and HDL ($r= -0.376$, $p< 0.05$) and significant but positive relationship between cholesterol and LDL ($r= 0.912$, $p<0.01$). Regarding G3; A significant direct correlation between BMI and serum TG ($r= 0.437$, $p<0.05$) and between cholesterol and LDL ($r=0.964$, $p<0.01$) can be noticed.

DISCUSSION

Iso et al (2009) reported that malignancy was associated with decreased plasma cholesterol levels, and certain types of cancer had a significant effect. The enhanced utilization of cholesterol by carcinoma tissues was the culprit in reducing plasma cholesterol. One of the important causes in the development of breast cancer is increased exposure to estrogen hormone which performs a vital role in cholesterol metabolism and may reflect the association of breast cancer and increased HDL (Llaverias et al, 2011). Although adjuvant chemotherapy may improve the survival of patients with breast cancer, they had suggested that chemotherapy gives rise to significant changes in lipids metabolism of tumor survivors (De Haas et al, 2010).

Alexopoulos et al (1992) found that breast cancer patients undergoing chemotherapy had a non-significant decline in both serum total cholesterol and serum LDL. Serum HDL did not show any significance while serum TG showed a significant increase. They had attributed these results to the decreased number of patients involved in the study and they had indicated that these lipid disorders could be reversed with the effective treatment of the tumor .

Seventy patients with breast cancer were studied by Rzymowska et al (1999), they had noticed that serum lipid profile was decreased after chemotherapy treatment along with a significant rise of serum triglycerides levels in malignant breast cancer women irrespective of being in menstruation or menopause. They had stated that the mechanisms interpreting chemotherapy-associated dyslipidemia could be related to the type of therapy used .

Other previous studies reported that HDL levels were significantly declined after chemotherapy and they had found that doxorubicin downregulates the expression of ATP binding cassette A1 transporter (ABCA1) as well as liver X receptor α (LXRα) and PPARγ (peroxisomal proliferator-activated receptor γ). While, paclitaxel or cyclophosphamide did not influence the level of ABCA1 (Sharma et al 2016; Basso et al, 2003) .

Recent studies reported that any chemotherapy that contains taxane can prompt dyslipidemia, which declines the plasma HDL level and raises the plasma hydroperoxide level (Yeo et al and Panis et al ,2017).

Alacacioglu et al. (2010) had observed that patients with breast cancer that were treated with cyclophosphamide, epirubicin and taxane exhibited no significant changes in blood cholesterol, HDL, LDL and TG at the baseline and after six cycles of the treatment.

Arpino et al. (2015) had studied the metabolic changes that occured in patients with breast cancer that were receiving adjuvant therapy and they had observed significant increases in serum cholestrol, LDL and TG levels.

In a study done by Simin et al. (2016) who found that patients treated with adriamycin, cyclophosphamide and taxane showed no significant changes in serum lipid profile although little changes were recorded in each item .

Xin et al. (2018) reported certain metabolic abnormalities during adjuvant chemotherapy treatment of women with breast cancer including hypercholesterolemia, hypertriglyceridemia; elevated LDL along with a decline in HDL. They proposed that breast carcinoma is associated with obvious dyslipidemia which gets worse after chemotherapy. These differences in the results may be due to the progress of cancer and side effects of the chemotherapeutic agents in addition to genetic, environmental, and behavioral differences (Peela et al, 2010).

The decrease in LDL in carcinoma could be attributed to increased uptake of cholesterol by these cells, with an eventual elevation in removing LDL through raising the activity of the LDL receptor. These derangements in lipid metabolism and parameters may be due to the release of pro-inflammatory cytokines from the inflammatory cells which could be part of an acute-phase reactant against tumor or which may be itself participate in tumor development and also from the tumor itself (Xin et al, 2018). The significant decrease in the serum HDL in this study was congruent with that stated by Sharma et al. (2016) who concluded that lipid changes that happened with chemotherapy are particular to the chemotherapeutic type used.

Also, Doxorubicin lowered HDL while paclitaxel increased apoB. In opposite, cyclophosphamide appears to have no significant effect on HDL or apoB metabolism. Some hypotheses indicate that chemotherapy may cause dysfunction of the endothelial cells which leads to cytokine alterations, and hence lipid abnormalities (Vehmanen et al, 2004; Ja et al, 2006) . Others stated that adipocytes associated with cancer will modify the phenotype of the cancer cells (Dirat et al,2011) .

Owiredu et al, (2009) had observed a positive and significant relationship between the body mass index and both total cholesterol and LDL which is more susceptible to lipid peroxidation. They had attributed this to the oxidative stress leading to an increase in cell proliferation of the malignant cells. Also, they had noticed a negative and significant relationship between age and HDL. This study was in concordance with the current study .

On the other hand; Delgobo et al. (2019) found that chemotherapy exerted major effects on the young patients with breast cancer and that sex hormones are correlated with the lipid metabolism . They had explained that alterations in serum lipid levels after chemotherapy is associated with alterations in menstruation. They had concluded that these alterations were due to the high level of sex hormones and the better lipid metabolism in these young patients (Vehmanen et al, 2004).

CONCLUSION

Iraqi women with breast cancer had mildly increased in LDL which exacerbated during chemotherapy treatment and resolved then after finishing the complete courses of treatment. These women showed a gradual decrease of HDL after treatment even its value still within the expected level.

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Conflict of interest: Nil.

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