

# Serum Lipid Profile in Iraqi patients with Breast Cancer

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## Abstract:

**Background:** Breast cancer (BC) is a type of cancer originating from breast tissue, Lipid profile seems to influence the development of female breast cancer, especially in the presence of an increased body mass index so.

**Objective:** to explore the status of lipid profile in women with breast cancer.

**Subjects and methods:** the present study is a cross-sectional study (2010/2011) done at Al-Yarmouk Teaching Hospital. Includes measurement of LP in sera of postmenopausal newly diagnosed women with BC in comparison with healthy control women. This measurement was done using colorimetric method. In The results of this study include a total of 100 patients with BC were involved in this study, they were classified as newly diagnosed postmenopausal women with BC G1: (n=100); together with 100 healthy Postmenopausal women as a control group G2: (n=100).

**Results:** Serum LP was significantly altered in newly diagnosed BC groups whom receive no therapy (G1) [ $P < 0.001$ ] when compared with control group (G2): this alteration was in term of significant increment in TC, TG, LDL and VLDL accompanied by elevation of HDL which was significant [ $P < 0.05$ ]

**Conclusion:** level of LP was significantly elevated in BC group suggesting atherosclerosis.

**Key words:** lipid profile, breast cancer.

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## Introduction:

Breast cancer has been researched world wide in recent years due to its high prevalence and incidence; it is the leading cause of cancer death among women [1], although advances in early detection and new therapeutic forms used have evolved over the last decades [2].

Among the aspects classically considered as risk factors for developing breast cancer are advanced age, low parity, early menarche, late menopause, obesity, alcoholism and increased height [3]. Among those linked to nutritional status, those related to body composition, such as obesity and/or overweight and inadequate distribution of body fat, especially in the post-menopause, are noteworthy [4].

Lipid profile seems to influence the development of female breast cancer, especially in the presence of an increased body mass index [5].

Proteins and lipids form specialized clusters in blood called as lipoproteins, which all tangled up together to carry lipids in our blood. These form fundamental component of cell membrane and play a vital role in cell growth and division and are also required for maintaining the cell integrity of normal and malignant tissues. Energy in the body is mainly

stored as triglycerides (TGs). TGs and cholesterol are first packed into lipoproteins and transported in plasma and later are taken up and degraded by cells for the cellular functions. Cholesterol, the known etiological factor of coronary heart disease, has recently become the focus of attention on the possible role in the etiology of cancer. Several authors propose that hypocholesterolemia to be a predisposing factor for cancer development [6, 7]. The aim of the present study is to assess the lipid profile levels in breast cancer women along with the normal subjects.

## Subjects and Methods:

**Subjects:** the study was a cross-sectional study carried out at Oncology Department at Al-Yarmouk Teaching Hospital, during the period from October, 2010 till the end of September, 2011. The protocol for the study was approved by the Ethical committee of Al-Nahrain Medical College, and informed signed consent was given by each subject. The study was conducted on patients with histologically confirmed hormone receptor-positive early-stage breast cancer. Additional inclusion criteria included: (a) no evidence of recurrent or metastatic disease; (b) postmenopausal women and (c) primary-treating oncologist approval.

The study include healthy postmenopausal, age-matched, women were also recruited for comparison purposes.

Patients with cardiovascular diseases, uncontrolled diabetes

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mellitus, acute hepatitis and nephrosis were excluded from the sample.

Blood samples: five milliliters of random venous blood were withdrawn from each patient and control after 12 hours fast. in supine position, without application of tourniquet. The samples were transferred into clean new plane tube, left at room temperature for 15 minutes for clotting, centrifuged at 1800 x g for 10 minutes at 4°C, and the separated serum was transferred into Eppendorf tube and was used for measurement of lipid profile. The tubes were stored at -20 C° until analysis,

which was done within one week after collection. [8].

#### Results:

Subjects: a total of 100 patients with BC were enrolled in this study who were newly diagnosed to have BC who receives no therapy for cancer (G1). The study included another 100 apparently healthy women, they were neither alcoholic nor smoker with no family history of any type of cancer who serve as healthy controls (G2); they were matched with patients' groups for age, sex, age of menarche, and Body mass index as in Table 1:

**Table (1): Clinical criteria of patient's groups with Breast Cancer & Control (presented as range and mean + SD).**

Group	No.	Age [range], Mea+n (SD) in years	Age at Menarche [range],mean (SD) in years	BMI [range],mean(SD)
G1	100	[57-69] years, 62± 7 years	[11-13.5] years, 11.7 ± 0.6 years	[23.5-32-2], 28.1 ± 3.5
G2	100	[55-66]years, 61±5 years	[12-14] years, 13.2±0.6 years	[20-30.5], 26 ± 4.3

Serum Lipid Profile: Serum LP was significantly altered in newly diagnosed BC groups whom receive no therapy (G1) [P < 0.001] when compared with control group (G2): this alteration was in term of significant increment in TC, TG, LDL and VLDL accompanied by reduction of HDL which was significant [P < 0.05] as in Table 2.

**Table (2): The mean serum Lipid Profile in different women with Breast Cancer and controls (presented as mean + SEM).**

Variable	No	TC(mmol/L)*	TG mmol/L*	LDL-C mmol/L*	HDL-C mmol/L**	VLDL-C mmol/L
G1	100	5.8 ± 1.6	2.7 ± 0.2	5.8 ± 1.6	1.06± 0.63	1.23 ± 0.23
G2	100	5.2 ± 0.4	2.6 ± 0.2	2.9 ± 0.5	1.15± 0.1	1.15 ± 0.63

G1): Postmenopausal women with BC: newly diagnosed, on no treatment.

(G2): Postmenopausal Healthy Controls.

\* t-test: G1 versus G2, p < 0.001

\*\* t-test: G1 versus G2, p < 0.05

#### Discussion:

Multiple epidemiological studies exploring causal associations between dyslipidemia and BC produced contradictory results [10, 11]. Several methodological aspects may explain the diverse conclusions, but the influence of cholesterol in BC risk remains to be clinical demonstrated. Nevertheless, biological clues from laboratory [12, 13] and in vivo pre-clinical studies [11, 12], as well as significant alterations in lipid profile of BC patients compared to healthy controls [14,15], are very suggestive for a role of cholesterol in BC.

To our knowledge this is the first cohort of Iraqi BC patients.

The correlation of lipid profile was done in a setting of pre-treatment and with all patients free of lipid lowering drugs. Despite we did not accessed variables that may also influence the lipid profile such as smoking habits, type of diet, residence

area or socioeconomic status, the most important co-variables, BMI, age and lipid lowering drugs were controlled.

In the present study, fasting lipid profile was prospectively assessed in a cohort of patients with breast carcinoma, in initial stages, before any treatment and with no history of being on antidiabetic or lipid lowering drugs (including statins, fibrates, oral antidiabetics, insulin or corticosteroids). Other published studies, also focused on assessing lipid profile in BC patients, found higher TC, LDL-C and decreased HDL-C levels in BC patients, compared to healthy control patients [15,16].

We found that LDL-C fraction is significantly associated with BC progression and may actually be useful in the identification and medical follow-up of high-risk groups. LDL-C levels at diagnosis therefore may emerge as a prognostic factor in BC patients.

As a limitation we could not avoid the possible influence of adjuvant treatment either in lipid profile or disease progression, once no modification to the routine protocols was introduced. It is also not possible to exclude the common association of cholesterol levels, obesity and the variance in health awareness before diagnosis. We can speculate that high LDL-C levels in patients with BC have a cancer-fuelling effect and are a co-causative factor, in patients with chronic hypercholesterolemia. But, on the other hand, the high LDL-C levels that we observed may actually reflect a shift in cholesterol synthesis (by the liver or tumor cells themselves) in patients with newly diagnosed tumors; accordingly, Zielinski et al. [17] followed-up a group of patients with advanced BC in remission and described a significant rise in plasma cholesterol and triglycerides in most of those who developed disease progression. Considering that proliferating cancer cells have an increased demanding of cholesterol and intermediates of cholesterol biosynthesis pathway, the up-regulation of cholesterol biosynthesis and reduced cellular efflux are expected. In cancer cells, cholesterol synthesis has been shown to be increased, due to availability of precursors or to increased transcription [18], and this may have contributed to BC carcinogenesis [18]. Hydroxy-3-methylglutaryl-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 [19] and acyl-CoA: cholesterol acyltransferase 1 inhibition, an enzyme involved in cholesteryl esterification decreases proliferation and invasion rate. However, despite cancer cells increases intracellular cholesterol synthesis, this effect is not expected to produce hypercholesterolemia and justify the observed associations [20]. So plasma LDL-C could be used by cancer cells. In vitro experiments, was also demonstrated that cancer cells can also consume HDL-C through the scavenger receptor class B, [15,16,17] and exogenous triglycerides [17]. In our clinical setting HDL-C or triglycerides measurements did not show suspicious modifications, but our results do not rule out the possibility of cancer cells consume. Corroborating this hypothesis are laboratory studies showing that both exogenous LDL-C and HDL-C can promote proliferation and migration, features of aggressive tumors [14-16]. Also animal studies showed a higher tumor and metastatic burden [11] as well as disease progression [12,13] in hypercholesterolemic mice compared with nonhypercholesterolemic controls. The exogenous cholesterol could be mobilized from body storage, through HDL-C or from diet, through hepatic metabolism and LDL-C.

High LDL-C and low HDL-C is the most common lipid profile induced by western diet and is highly frequent [8]. Initial studies on cholesterol and cancer showed an increased risk in patients with lower plasma cholesterol; however, assuming that cholesterol is essential to cell proliferation, once a tumor

develops in a hypercholesterolemic environment it is well adapted to progress and this may be the explanation for the observed elevation of LDL-C level and disease progression [12-14].

### Conclusion

In this study TC, LDL, Triglyceride level analysis showed significantly higher levels BC patients than that of the controls, whereas HDL showed significant lower level. Higher VLDL levels were observed in BC patients than the control group. These alterations in the plasma lipid profile patterns were significant and recommend a still in-depth study in this aspect for early diagnosis and management of breast cancer.

### Author's contributions:

Dr. Faisal Gh. Al-Rubaye : study conception and design

Dr. Taha Sh. Morad : Acquisition of data

Dr. Mohammed I. Hamzah :Analysis and interpretations of data

Dr. Shatha M. Hasan , Dr. Taha Sh. Morad, Dr. Faisal Gh. Al-Rubaye: drafting of manuscript.

Dr. Mohammed I. Hamzah and Dr. Faisal Gh.: critical revision

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