Assessment of lipid profile parameters in women with benign and malignant breast tumor

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Abstract

The cause of breast cancer remains unknown, but numerous factors have been directly associated with increased risk of breast cancer incidence. Among them lipid profile is one of the most important risk factors that may directly associate with breast cancer prevalence and incidence. The objective of this study is to assess lipids profile parameters in women with breast tumor and investigate their role in breast tumor initiations. A case control study was done on105 women range from 35 -70 years that had breast tumor. Lipids profile parameters were measured in serum of women who were categorized as newly diagnosed with untreated malignant breast tumor (n=35), newly diagnosed untreated women with benign breast tumor (n=35) and comparable age healthy women that considered as a control group (n=35). There were significant increases in the levels of TC and LDL-C in patients with malignant tumor in comparison with both benign group and controls, while TG and VLDL levels were significantly elevated in patients with malignant breast tumor in comparison only with control group. Receiver Operating Characteristic (ROC) curve showed that TC and LDL-C levels showed high sensitivity and specificity with high area under curve in malignant condition. In conclusions, lipids profile parameters especially TC and LDL-C may have a direct role in breast cancer initiation, progression and metastasis.

Key words: Lipid profile; Breast cancer; Total cholesterol; Total triglyceride

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Introduction

Breast cancer known as cancer that develops from breast tissues. Breast cancer most commonly develops in cells from the lining of milk ducts and the lobules that supply the ducts with milk [1]. Cancers developing from the ducts are known as ductal carcinomas, while those developing from lobules are known as lobular carcinomas. About 5–10% of cases are due to gens inherited from person's parents. American Cancer Society estimated

that 252,710 invasive breast cancers discovered in women in the United States in 2017 and there were 40,610 deaths, making this fatal second only to lung cancer as a cause of cancer death in women [2]. Breast cancer usually first detected as palpable mass or as mammographic abnormality, but also can be manifested initially by nipple discharge, breast skin change, or breast pain [3]. Many risk factors well known to increase the incidence of breast cancer initiation like Age, gander, personal history of breast cancer and a family history of breast cancer have the greatest relative factors [4]. Many studies have indicated the correlation of lipids and lipoproteins with the risk of breast cancer. The exact mechanisms by which lipids, lipoproteins contribute to carcinogenesis are not clearly understood [5]. Previous studies reported that there were elevation of TC and TG levels in breast cancer [6, 7]. They suggested that cholesterol may apparently stimulate cell proliferation and induce fibrosarcoma's. Also suggests that higher concentration of TG may lead to the decreased level of sex hormone-binding globulin, which may likely to increase breast cancer risk. Recent studies also propose that higher concentrations of TC and TG may either play a role in carcinogenesis or are responsible for higher incidence of breast cancer [8].

Materials and Methods

A case control study was done on 70 women range from 40 -70 years who had breast tumor recruited from Operations Hall in general surgery Department at Al Imamain Al-Kathemeaain medical city, Baghdad, Iraq. Thirty-five newly diagnosed untreated women with malignant breast tumor (approved by histopatholgist) aging 40-70 years (mean + SD 49.7±3.2). Thirty-five newly diagnosed untreated women with benign breast tumor (approved by histopatholgist) aging 40-70 years (mean + SD 47.28±2.89). The results of the patients groups were compared with Thirty five comparable age (mean +SD 45.92±2.59) healthy women have no breast tumor or other breast complication before used as a control group with executions criteria includes Women age more than 70 years and less than 35 years, Have tumors anywhere other than breast and Women have history of breast tumors and get treated before for any breast complications. Five milliliters of blood were put into serum separating tube (SST) and left to clot for 15-30 min at room temperature then were centrifuged at 8000 rpm for 15 min, the separated sera were divided into small aliquots and store at (-20oC) until assayed for the evaluation of lipids profile (Total cholesterol, triglyceride, VLDL, LDL and HDL).

The study was approved by the local Ethical Committee of the College of Medicine, Al-Nahrain University, Baghdad, Iraq. In addition, an informed written consent for participation

in the study was signed by the participant or the legal guardians of the investigated subjects according to the Helsinki principles.

Statistics

Results were expressed as mean ± standard deviation (SD) and all statistical comparisons were made by means of independent t-test and Analysis of variance (ANOVA) test with P ≤0.05 was considered statistically significant. The correlation was done between all parameters using Pearson correlation test. All statistical analysis was carried out using Statistical Package for the Social Sciences (SPSS) software 20. Receiver Operating Characteristic (ROC) analysis was performed as a comprehensive way to assess the accuracy of the studied markers. The area under the curve (AUC) provides a useful tool to compare different biomarkers. Whereas an AUC value close to 1 indicates an excellent diagnostic and predictive marker, a curve that lies close to the diagonal (AUC = 0.5) has no diagnostic significance. AUC close to 1 is always accompanied by satisfactory values of specificity and sensitivity of the biomarker.

Results

Some demographic characteristics of the studied groups were summarized in table 1.

Table 1 showed non-significant differences in age and body mass index (BMI) among all studied groups.

Table 1.

Demographic characteristics of the autistic patients and control

	Control	Benign breast tumor	Malignant breast tumor
N	35	35	35
Age	45.92±2.59	47.28±2.89	49.7±3.2
P-value with control		0.74	0.24
Weight	69.62±8.76	71.22±9.21	74.45±10.07
Height	161.5±14.39	159.42±13.6	158.7±14.55
BMI	26.36±4.89	27.82±5.05	28.53±5.34
P-value with control		0.54	0.15

According to results presented in table (2), there were non-significant differences between control subjects and patients with benign tumor in the levels of total cholesterol and triglycerides (p=0.214 and p=0.928, respectively) and also a non-significant difference in the level of TG between patients with benign and malignant tumor (p=0.069). On the other hand, significant increases in the levels of TC were observed in both patients with benign and malignant tumor in comparison with controls. Furthermore, the level of TC in patients with malignant tumor showed to be significantly higher than that in patients with benign tumor (p<0.001). Additionally, ANOVA test also revealed that there were significant differences in the levels of both TC and TG among the studied groups (p<0.001 and p=0.008, respectively).

Table 2.

Total Cholesterol and Triglyceride levels in controls, patients with benign and malignant breast tumor

	Group	mean±SD	P^a	P^b	P^c	P^d
Total cholesterol (mg/dl)	Control n= 35	115.3±11.89	0.214	<0.001	<0.001	<0.001
	Benign tumor n=35	127 ± 15.03				
	Malignant Tumor n=35	158.11± 32.01				
Triglyceride (mg/dl)	Control n= 35	65.19±14.58	0.928	0.011	0.07	0.008
	Benign tumor n=35	67.5±12.92				
	Malignant Tumor n=35	80.72±27.99				

Pa value between patients with benign tumor and control.
Pb value between patients with malignant tumor and control
Pc value between patients with benign tumor and patients with malignant tumor
Pd value among all studied group (ANOVA test)

The pattern of HDL, LDL and VLDL levels were varied among the studied group as illustrated in table (3). Firstly, HDL levels showed non-significant differences among all studied groups whereas the levels of LDL and VLDL showed some similarities in their pattern with the previously described TC and TG, respectively, that indicated by the non-significant differences between controls and patients with benign tumor in the levels of LDL and VLDL (p=0.93 and p=0.9, respectively) and also a non-significant difference between patients with benign and malignant tumor in the level of VLDL. On the other hand, significant increase in the levels of LDL and VLDL were noticed in patients with malignant breast tumor in comparison with controls. Moreover, results obtained by ANOVA test revealed that there were significant differences in the levels of both LDL and VLDL among the studied groups.

Pearson correlation results illustrated in tables 4,5 and 6 revealed that in controls, correlations among lipid profile parameters showed significant positive correlations between cholesterol levels and both LDL and VLDL levels (r=0.795; p<0.001 and r=0.453; p=0.045, respectively) in addition to positive correlations between TG levels and both LDL and VLDL levels (r=0.491; p=0.028 and r=0.934; p<0.001, respectively) beside a significant positive correlation between LDL and VLDL levels (r=0.516; p=0.02) as illustrated in table 4. Furthermore, correlations among lipid profile parameters in patients with benign mass showed significant positive correlations between cholesterol levels and TG, LDL and VLDL levels (r=0.509; p=0.005, r=0.628; p<0.001 and r=0.507; p=0.005, respectively) in addition to positive correlations between TG levels and VLDL levels (r=0.95; p<0.001) beside a significant negative correlation between LDL and HDL levels (r= -0.827; p<0.001) as shown in table 5. Moreover, correlations among lipid profile parameters showed significant positive correlations between cholesterol levels and all other lipid profile parameters including TG, HDL, LDL and VLDL levels (r=0.717; p<0.001, r=0.451; p=0.003, r=0.61; p<0.001 and r=0.719; p<0.001, respectively) in addition to positive correlations between TG levels and both HDL and VLDL levels (r=0.918; p<0.001, r=0.924; p<0.001) beside a significant positive correlation between VLDL and HDL levels (r= 0.917; p<0.001) and negative correlation between LDL and HDL levels (r= -0.431; p=0.005) that demonstrated clearly in table 6.

Table 3.

HDL, LDL and VLDL levels in controls, patients with benign and malignant breast tumor

	Group	mean±SD	P^a	P^b	P^c	P^d
HDL (mg/dl)	Control n= 35	52.21±10.07	0.06	0.537	0.255	0.063
	Benign tumor n=35	39.88± 16.43				
	Malignant Tumor n=35	46.91± 21.98				
LDL (mg/dl)	Control n= 35	61.31±14.7	0.93	<0.001	<0.001	<0.001
	Benign tumor n=35	63.73±18.33				
	Malignant Tumor n=35	94.95±29.45				
VLDL (mg/dl)	Control n= 35	12.96±2.91	0.9	0.009	0.07	0.007
	Benign tumor n=35	13.5±2.58				
	Malignant Tumor n=35	16.12±5.59				

Pa value between patients with benign tumor and control.
Pb value between patients with malignant tumor and control
Pc value between patients with benign tumor and patients with malignant tumor
Pd value among all studied group (ANOVA test)

In addition to t-test results and correlations demonstrated above, ROC curve analysis also revealed that lipid profile parameters showed a low specificity and sensitivity with low AUC values between patients with benign tumor and healthy volunteers subjected to the current study as obtained in table 7. On the contrary, comparing lipid profile parameters in patients with malignant tumor with those of benign tumor revealed that total cholesterol and LDL levels showed a relatively high AUC value (0.876, 0.806, respectively) with a satisfactory value of accuracy presented as specificity (83% and 65.5%, respectively) and sensitivity (81% and 80.5%, respectively) while TG, HDL and VLDL levels showed low values of AUC with low sensitivity and specificity as illustrated in table 8.

Table 4.

Correlations between the levels of all studied parameters among control subjects

		Cholesterol	TG	HDL	LDL	VLDL
Cholesterol	r	1	.437	.216	.795**	.453*
	p		.054	.359	.000	.045
TG	r	.437	1	-.320	.491*	.934**
	p	.054		.169	.028	.000
HDL	r	.216	-.320	1	-.406	-.332
	p	.359	.169		.076	.153
LDL	r	.795**	.491*	-.406	1	.516*
	p	.000	.028	.076		.020
VLDL	r	.453*	.934**	-.332	.516*	1
	p	.045	.000	.153	.020	

Table 5.

Correlations between the levels of all studied parameters among patients with benign breast tumor

		Cholesterol	TG	HDL	LDL	VLDL
Cholesterol	r	1	.509*	-.126	0.628	0.507
	p		.005	.515	.000	.005
TG	r	.509**	1	-.159	.228	0.95
	p	.005		.411	.235	.000
HDL	r	-.126	-.159	1	-.827	-.159
	p	.515	.411		.000	.409
LDL	r	0.628	.228	-.827	1	.227
	p	.000	.235	.000		.236
VLDL	r	0.507	0.95	-.159	.227	1
	p	.005	.000	.409	.236	

Table 6.

Correlations between the levels of all studied parameters among patients with malignant breast tumor

		Cholesterol	TG	HDL	LDL	VLDL
Cholesterol	r	1	.717**	.451**	.610**	.719**
	p		.000	.003	.000	.000
TG	r	.717**	1	.918	-.097	0.924
	p	.000		.000	.545	.000
HDL	r	.451**	.918*	1	-.431	.917
	p	.003	.000		.005	.000
LDL	r	.610**	-.097	-.431	1	-.096
	p	.000	.545	.005		.552
VLDL	r	.719**	0.924	.917	-.096	1
	p	.000	.000	.000	.552	

Table 7.

ROC curve results for all studied parameters in patients with benign breast tumor comparing with controls

Parameters	AUC	Sensitivity (%)	Specificity (%)	Cut-off value
Cholesterol	0.723	75	62	119.23
TG	0.547	50	62	70.51
HDL	0.714	75	66	44.37
LDL	0.53	66	60	58.84
VLDL	0.557	50	62	14.02

Table 8.

ROC curve results for all studied parameters in patients with malignant breast tumor comparing with benign breast tumor patients

Parameters	AUC	Sensitivity (%)	Specificity (%)	Cut-off value
Cholesterol	0.876	81	83	137.43
TG	0.642	58.5	62.1	70.92
HDL	0.578	48.8	62.1	43.49
LDL	0.806	80.5	65.5	74.57
VLDL	0.650	58.5	65.5	14.24

Furthermore, ROC curve analysis results for lipid profile parameters in women with a malignant tumor in comparison with those in patients with benign masses revealed that total cholesterol and LDL levels showed a relatively high AUC value (0.777, 0.877, respectively) with a satisfactory values of accuracy presented as specificity (85% and 75%, respectively) and sensitivity (68% and 90.2%, respectively) whereas TG, and VLDL showed low values of AUC with low sensitivity and specificity as illustrated in table 9. Moreover, HDL level showed a unique pattern in which low AUC and specificity values were noticed (0.63 and 51.2%; respectively) with a high sensitivity value (100%).

Table 9.

ROC curve results for all studied parameters in patients with malignant breast tumor comparing with controls

Parameters	AUC	Sensitivity (%)	Specificity (%)
Cholesterol	0.777	68.3	85
TG	0.606	58.5	65
HDL	0.63	100	51.2
LDL	0.877	90.2	75
VLDL	0.604	56	65

Discussion

Many attempts were conducted to clarify the role of lipid profile assessment in diagnosis, prognosis and determine the pathogenesis of breast tumors. Total cholesterol (TC) levels in the current study showed to be significantly increased in patients with malignant breast tumor when compared with benign breast tumor patients and matched age /sex healthy control subjects which is in consistency with Nelson et al 2014 who demonstrated that cholesterol have clear pathological actions in breast tumor growth. The expected explanation of the role of high cholesterol level in breast cancer is compatible with the hypothesis about the role of cholesterol as a risk factor in breast tumors initiation by which dyslipidemia results in increased cholesterol content in cell membranes thus impacting membrane fluidity and subsequent signaling in cell membrane that may promote tumors angiogenesis [9]. Furthermore, study conducted by Llaverias et al., 2011 [10] demonstrated that increased plasma cholesterol, in association with oncogenic stimuli, lead to accelerated tumor formation and increased tumor burden. Additionally, from table 2 there is a significant

difference in cholesterol level in patients with malignant breast tumor as compared with benign ones in agreement with results obtained by His et al., 2017 [11]. Moreover, table 2 also showed that there are non-significant differences in total cholesterol level between those with benign breast tumor and healthy control women as in consistency with Chandler et al., 2016 [12]. Receiver Operating Characteristic (ROC) curve for total cholesterol showed low sensitivity and specificity in benign breast tumors group when compared with healthy subjects which confirm the above results in that there is a non-significant difference between these two groups. While ROC curves for total cholesterol in malignant breast tumors group showed good sensitivity and specificity when compared with patients with benign tumor and heathy controls in agreement with the above-mentioned results.

Total cholesterol has important role in breast tumors initiation and growth and considered as one of most obvious breast mass risk factors as described recently in several studies [13,10]. Regarding TG levels, result showed in table 2 revealed that there was only significant elevation in TG level in patients with malignant breast cancer as compared with control matched comparable (age/sex) groups. Which have similarities with results of other [6], while a non-significant differences were noticed in TG levels between malignant and those with benign breast tumors that is greatly agreed with Chen et al., 2016 [14] study and also between benign breast tumor patients and healthy controls which is disagree with previous study which postulated that there were significant differences in TG levels between benign breast tumor patients and comparable healthy control women which exclude the consideration of hyper-triglyceridemia as a tumor marker as it increased in both malignant and benign patients in a comparable manner that makes it difficult to distinguish between them by this test [15].

The possible explanation of these controversial results may be owned to that Yang and his colleagues study conducted on six benign patients only, so, this result needs further investigations with a larger sample size as the current study did. ROC curve for triglyceride showed low sensitivity and specificity with small area under the curve in malignant group when compared with both benign breast tumor patients and control subjects and also low sensitivity and specificity between the benign breast tumor patients and control subjects that confirm the above presented results which assumed that TG levels cannot be used as a reliable test for tumor diagnosis and differentiation.

In current study, there was a non-significant differences in concentration of HDL in all studied groups in addition to ROC curve results that also revealed low sensitivity and specificity among all studied group which means that HDL have no role in breast tumors initiation and progressions as suggested earlier by several researches [16, 17]. In a parallel with results obtained for TC, the present study showed significant elevations in the levels of

LDL in malignant breast tumors patients when compared with both benign breast tumors and control subjects as see in table 3. These results greatly supported by Mishra, 2015 who demonstrated that LDL-cholesterol levels significantly increased in patients with breast cancer when compared with the controls. Mishra, 2015 [18] also assumed that the elevated serum LDL-cholesterol levels contribute to its more susceptible to oxidation that may result in high lipid peroxidation in breast cancer patients.

This may generate an oxidative stress leading to cellular and molecular damage thereby resulting in cell proliferation and malignant conversions. Additionally, the results of table 3 showed that there were non- significant differences in levels of LDL between benign breast tumors and control groups. ROC curve results for LDL showed high sensitivity and moderate specificity (90.2%, 75% respectively) with high AUC (0.877) in patients with malignant breast tumors when compared with control subjects. Whereas, a moderate sensitivity and specificity was obtained between patients with malignant and benign breast tumor.

These results beside those obtained for total cholesterol explain the role of the cholesterol carrier “LDL” as a risk factor for breast cancer initiations. Results presented in table 3 clarified that VLDL levels showed a pattern similar to that of triglyceride in which only significant elevation in VLDL level presented in malignant breast tumors group when compared with both benign and control group in agreement with that obtained in previous literatures [19, 20]. Furthermore, there is non-significant differences in VLDL levels between malignant and benign groups and also between benign and control groups.

Additionally, ROC curve results confirm the non-significant differences in VLDL levels among all studied groups by low sensitivity and specificity with small AUC between these groups. The correlations between lipid profile parameters (total cholesterol, total triglyceride, HDL, LDL, and VLDL) in both benign breast tumor group and healthy control subjects showed positive correlations between TC and both LDL and VLDL and also between TG and VLDL. In addition to that there was a positive significant correlation between LDL and VLDL in controls.

There is no other correlation seen between TC and any lipid profile parameters other than LDL, and between TG and any lipid profile parameters other than VLDL. HDL showed non-significant correlations with any other lipid profile parameters. All these results seen in tables (4 and 5). These results supported by many previous studies [17, 21-22]. All these studies agreed on that elevation in serum total cholesterol, Triglyceride, LDL-C and VLDL may enhance the risk for breast tumors occurrence. In current study, the correlation between lipid profile parameters in malignant breast tumors showed that there were high positive correlations between TC and TG, LDL, HDL and VLDL. Moreover, triglyceride showed

positive correlations with HDL and VLDL. These results are comparable with many previous studies that approve these positive significant correlations among patients with breast cancer which in turn confirm the possible participation of lipid profile parameters in pathogenesis and progression of breast cancer [21-24].

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Ethical Approval

The study was approved by the Ethical Committee.

Conflicts of Interest

The authors declare that they have no competing interests.

Authors' Contributions

Both authors shared in conception, design of the study, acquisition of data, and manuscript writing, the critical revising and final approval of the version to be published.

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