Asian Pacific Journal of Cancer Care
Vol 10 No 2 (2025), 451-456
Original Research

Effect of Tamoxifen Treatment on Lipid Profile in Hormone Receptor Positive Breast Cancer Women in Duhok City: A Cross-Sectional Study

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Objectives: Tamoxifen's anti-estrogenic properties may have an impact on lipid metabolism; therefore, each patient's risk-benefit profile must be carefully considered. This study examines how tamoxifen affects Kurdish women's lipid profiles.

Methods: The study is conducted on 120 females with (ER and /or PR) positive breast cancer on adjuvant hormonal therapy with tamoxifen (in a dose 20 mg once daily) for 3 months and more, at Azadi Hematology Oncology Center, Duhok city.

Results: In this study, TG and VLDL-C are shown to increase with rising age and BMI. In contrast, all BMI categories show consistently reduced levels of HDL-C. Furthermore, TC levels were reduced but within the reference ranges in elder individuals, and the TC/HDL-C ratio rose with increasing BMI within the reference ranges.

Conclusion: Healthcare professionals are encouraged to routinely check the lipid profiles of these patients and suggest lifestyle modifications. The long-term effects of tamoxifen on lipid metabolism, especially in larger populations, require more investigation.

Introduction

Globally, the prevalence of breast cancer (BC) is rising quickly [1]. After skin cancer, BC is one of the most prevalent cancers in women in the United States. The lifetime risk of BC for women is 12.9%, and the disease's incidence is rising at a rate of 0.5% annually [2].

Anti-estrogen treatments will benefit nearly two-thirds of female BC patients who have expression of estrogen (ER) and/or progesterone receptors [3]. For non-metastatic BC, tamoxifen, a non-steroidal medication, is utilized in adjuvant hormonal therapy. This selective estrogen receptor modulator (SERM) does not alter the synthesis of estrogen, instead it prevents estrogen from attaching to the estrogen receptor [4]. Because SERMs function as both agonists and antagonists of estrogen receptors in different tissues, they are referred to as "modulators" of estrogen receptors rather than "agonists" or "antagonists" [5].

The therapeutic response to tamoxifen varies significantly between individuals, which may be caused by environmental and/or genetic factors that change the drug's concentration and the plasma levels of its active metabolites [6]. For example, there were notable differences in the plasma concentrations of the drug and its active metabolites due to menopausal status, body mass index (BMI), circadian rhythm, usage of other medications, concurrent meal consumption, and non-adherence to treatment [7].

According to several clinical and experimental studies, tamoxifen has a significant estrogenic action that lowers cholesterol levels and may lower the risk of myocardial infarction [8]. Thus, by altering lipid metabolism, tamoxifen may reduce the risk of cardiovascular disease (CVD) and related mortality in addition to its anti-estrogenic effect. Tamoxifen has been linked to a decrease in the amount of low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), and triglycerides (TG) in the blood [9]. However, there are no clinical recommendations for using tamoxifen to reduce TG or TC [10].

Therefore, we aim to assess the impact of tamoxifen on plasma lipids to determine the change in serum lipid profile in non-metastatic hormone receptor positive BC Kurdish women, treated with adjuvant tamoxifen; in Duhok city.

Materials and Methods

Study Design

The study is a prospective cross-sectional study carried out from October, 2024 till the end of January, 2025. It is conducted on 120 females with (ER and /or PR) positive BC on adjuvant hormonal therapy with tamoxifen (in a dose 20 mg once daily) for 3 months and more, at Azadi Hematology Oncology Center (AHOC), Duhok city. The protocol for the study was approved by the local research ethics committee of Duhok Directorate General of Health registered as the reference number (25092024-8-16) in 16th August, 2024.

Inclusion Criteria

Non-metastatic BC patients irrespective of menopausal state who receive tamoxifen therapy for three months and more.

Exclusion Criteria

The patients recently had done the radiation and/ or surgery. Male patients. Patients with lipid reduction medications, diabetes mellitus, thyroid dysfunction, hepatic or renal impairment, hypertensive patients on those therapy which have impact on lipid profile (beta-blocker and thiazide), and smoker patients were excluded.

Blood Samples

Two milliliters of random venous blood were withdrawn from each patient after 9-12 hours fasting in fowler’s position, with application of tourniquet. The samples were transferred into clean serum separating tube (Gold Tube), wait 30-60 minutes to be clotted. The samples are centrifuged for 10 minutes to separate the plasma or serum from the blood cells. The separated serum is then analyzed in a laboratory using Cobas c501 module (Roche Cobas 6000 Diagnostics, Germany) automated machine.

Sampling

This study enrolled all patients (according to inclusion criteria) who have taken tamoxifen for three months and more by the measurements of lipid profile biomarkers: TC, High-density Lipoprotein-

Cholesterol (HDL-C), LDL-C, TG.

And calculated: Very Low-density Lipoprotein- Cholesterol (VLDL-C), TC/HDL-C Ratio, LDL-C/ HDL-C Ratio by the following formulas:

VLDL (mg/dL) = TG/ 5

TC/HDL-C Ratio = (Total Cholesterol)/(HDL-C) LDL-C/ HDL-C = (LDL-C)/(HDL-C)

In this study, WHO classification of BMI was used as following: 18.5-24.9 Kg/m^2, 25-29.9 Kg/m^2 overweight, and 30 Kg/m2 and above obese [11]. BMI is calculated by the following formula:

BMI (Kg/m^2) = Weight (Kg)/Height (m^2)

Statistical Analysis

Comparisons with each patient's pre-treatment levels were not possible in this study since the participants did not have access to baseline (pre-treatment) lipid profile data. Rather, comparisons within study population subgroups (based on age, BMI, and length of tamoxifen treatment) were the main focus of the research. To determine if measured results fell within normal bounds, lipid measurements were also analysed in relation to accepted clinical reference ranges. Each patient assigned a serial identification number. Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) version 30. Basic descriptive statistics, including means, standard deviations (SD), median, interquartile range (IQR), and percentages, were used to characterize the study participants. Statistically significant differences between subgroups were assessed using descriptive and inferential statistics (ANOVA or Kruskal-Wallis test, if appropriate). All statistical tests were two-sided and the level of significance (alpha) was set at $P< 0.05$ (5%).

Results

Overall, 150 patients were initially included in the study who are treated in Duhok city, only 120 were included in the analysis, 30 patients were excluded due to the exclusion criteria. The demographic and laboratory parameters of the study population are shown in (Table 1).

Variables			Statistical Values
Age (Years) (%)		Mean Age ± SD	42.38 ± 6.61
		< 40 Y	34 (28.3)
		40-49 Y	68 (56.7)
		50-59 Y	18 (15)
BMI (Kg/m2) (%)		Mean BMI ± SD	28.7 ± 4.86
		Normal: 18.5-24.9	29 (24.2)
		Overweight: 25-29.9	46 (38.3)
		Obese: ≥ 30	45 (37.5)
Marital Status No. (%)		Married	100 (83.3)
		Unmarried	20 (16.7)
Parity No. (%)		Nulli	28 (23.3)
		Multi	92 (76.7)
Occupation No. (%)		Employed	23 (19.2)
		Unemployed	97 (80.8)
Family History No. (%)		Yes	79 (65.8)
		No	41 (34.2)

Surgery Type No. (%)		Lumpectomy	80 (66.7)
		Mastectomy	40 (33.3)
Duration of Disease (Months) (%)		≥24	65 (54.1)
		< 24	55 (45.9)
Duration of Tamoxifen Treatment (Months) (%)		3-9	26 (21.7)
		10-16	21 (17.5)
		17-23	21 (17.5)
		≥24	52 (43.3)
Variables Mean ± SD		Reference Ranges	Statistical Values
	TC	120-200 (mg/dL)	186.33 ± 37.36
	HDL-C	40-60 (mg/dL)	49.92 ± 11.39
	LDL-C	50-100 (mg/dL)	102.36 ± 33.58
Lipid Profile Biomarkers	TC/HDL-C	3.5-6.9	3.88 ± 0.99
	LDL-C/HDL-C	1.2-6.2	2.13 ± 0.78
Variables Median (IQR)		Reference Ranges	Statistical Values
	TG	35-150 (mg/dL)	160.95 (109.5-245)
	VLDL-C	13-25 (mg/dL)	32.19 (21.9-49)

Table 1. The Demographic and Laboratory Characteristics of the Study Population.

Abbreviations, (BMI) Body Mass Index, (TC) Total Cholesterol, (HDL-C) High-density Lipoprotein Cholesterol, (LDL-C) Low-density Lipoprotein Cholesterol, (TC/HDL-C) Total Cholesterol/ High-density Lipoprotein Cholesterol Ratio, (LDL-C/HDL-C) Low-density Lipoprotein Cholesterol/ High-density Lipoprotein Cholesterol Ratio, (TG) Triglycerides, (VLDL-C) Very Low-density Lipoprotein Cholesterol, (SD) Standard Deviation, (IQR) Interquartile Range, (Kg/m^2) Kilograms per Square Meter, (mg/dL) Milligrams per Deciliter.

The Table 1 also shows other characteristics which were collected through a questionnaire, including: Age, BMI, marital status, parity, occupation, family history of cancer, surgery type, duration of disease, and duration of tamoxifen treatment.

The mean age of participants was 42 years old. The mean BMI was (28.7 Kg/m^2), from the 120 patients, 29 patients had normal BMI (24.2%), 46 patients were overweight (38.3%), and 45 patients were obese (37.5%). The median duration of tamoxifen treatment was 20 (11-31) months.

The patients were divided into subgroups based on age, BMI and duration of tamoxifen treatment. In (Table.2), the relation between age groups and lipid biomarkers (TC, HDL-C, LDL-C, TC/HDL-C, and LDL-C/HDL-C ratios) are shown. The TC levels are decreased in all age groups and they were statistically significant ($p<0.05$), but those reducing levels were remained within the reference ranges. The changes of other lipid parameters are not statistically differed among all age groups ($p>0.05$).

In (Table 2), the relation between BMI and lipid biomarkers (TC, HDL-C, LDL-C, TC/HDL-C, LDL-C/

HDL-C) are shown. The HDL-C levels are reduced but remained within the reference ranges with higher BMI of patients and those changes are highly statistically significant ($p<0.001$). Also, TC/HDL-C ratios are increased but remained within the reference ranges with higher BMI, and they are statistically significant ($p<0.05$).

While the other differences of lipid levels with BMI are not statistically significant ($p>0.05$).

In the levels of (TC, HDL-C, LDL-C, TC/HDL-C, LDL-C/HDL-C), there are no differences when

comparing their levels with the duration of treatment of tamoxifen which are classified into four groups (3-9, 10-16, 17-23, ≥24) months of duration. No significant differences found with increasing the duration of Tamoxifen treatment (p>0.05), shown in (Table 2).

Variable							Lipid Biomarkers								
Age Group (Years)	TC (mg/dL)			HDL-C (mg/dL)			LDL-C (mg/dL)			TC/HDL-C			LDL-C/HDL-C		
	Mean	SD	Sig.	Mean	SD	Sig.	Mean	SD	Sig.	Mean	SD	Sig.	Mean	SD	Sig.
< 40	192.088	41.3		53.22	11.71		109.91	36.67		3.72	0.95		2.16	0.85	
40-49	188.429	35.6	0.04	48.67	11.35	0.159	102.18	31.73	0.111	4.04	1.03	0.091	2.18	0.76	0.227
50-59	167.55	31.81		48.46	10.19		88.79	31.72		3.57	0.82		1.87	0.66	
Total	186.33	37.36		49.92	11.39		102.36	33.58		3.88	0.99		2.13	0.78	
Variable							Lipid Biomarkers								
BMI	TC (mg/dL)			HDL-C (mg/dL)			LDL-C (mg/dL)			TC/HDL-C			LDL-C/HDL-C		
(Kg/m2)															
	Mean	SD	Sig.	Mean	SD	Sig.	Mean	SD	Sig.	Mean	SD	Sig.	Mean	SD	Sig.
18.5-24.9	191.28	40.43		56.14	11.09		107.58	30.12		3.47	0.82		1.96	0.6	
25-29.9	190.8	37.13	0.213	50.5	11.16	<0.001	103.21	34.18	0.49	3.93	1.03	0.029	2.15	0.88	0.372
≥30	178.58	35.02		45.32	9.89		98.14	35.22		4.09	1		2.21	0.77	
Total	186.33	37.36		49.92	11.39		102.36	33.58		3.88	0.99		2.13	0.78	
Variable							Lipid Biomarkers								
Tamoxifen Duration (Months)	TC (mg/dL)			HDL-C (mg/dL)			LDL-C (mg/dL)			TC/HDL-C			LDL-C/HDL-C		
	Mean	SD	Sig.	Mean	SD	Sig.	Mean	SD	Sig.	Mean	SD	Sig.	Mean	SD	Sig.
3-9	185.97	32.66		50.39	11.34		104.72	31.59		3.85	1.05		2.19	0.86	
10-16	192.71	30.15		51.57	12.99		111.01	30.64		3.93	0.99		2.24	0.66	
17-23	173.29	37.28	0.311	51.18	13.79	0.69	94.61	35.51	0.429	3.55	0.99	0.376	1.95	0.86	0.662
≥24	189.21	41.68		48.52	9.75		100.82	34.91		4	0.97		2.12	0.75	
Total	186.33	37.36		49.92	11.39		102.36	33.58		3.88	0.99		2.13	0.78	

Table 2. Association of Age Groups, BMI, and Tamoxifen Duration Treatment with Serum Lipid Biomarkers in Hormonal BC Women.

Abbreviations, (BMI) Body Mass Index, (TC) Total Cholesterol, (HDL-C) High-density Lipoprotein Cholesterol, (LDL-C) Low-density Lipoprotein Cholesterol, (TC/HDL-C) Total Cholesterol/ High-density Lipoprotein Cholesterol Ratio, (LDL-C/HDL-C) Low-density Lipoprotein Cholesterol/High-density Lipoprotein Cholesterol Ratio, (SD) Standard Deviation, (Kg/m^2) Kilograms per Square Meter, (mg/dL) Milligrams per Deciliter, (Sig.) Significance.

For TG and VLDL-C, the median and IQR for both lipid biomarkers are compared and Kruskal-Wallis (H-test) is used to determine the significant changes between them. In (Table 3), the level of TG and VLDL-C are increasingly higher than normal in age groups (40-49, 50-59) years old, and that high level is statistically significant ($p<0.05$). Table 3 has shown that TG and VLDL-C levels are increasingly higher than normal with higher BMI categories which are statistically significant. Median TG is higher than normal in the patients who has taken tamoxifen treatment for (≥24) months, and median VLDL-C levels are higher than reference ranges in all categories of tamoxifen duration, but those differences are not statistically significant ($p>0.05$), shown in (Table 3).

Variable		Lipid Biomarkers			Significance
Age Groups (Years)	TG (mg/dL)		VLDL (mg/dL)		
	Median	IQR	Median	IQR	
< 40	126	109	25.2	21.75	
40-49	193	148	38.6	29.75	0.022
50-59	158.95	133.75	31.79	26.75	
Total	160.95	135.5	32.19	27.1	
Variable		Lipid Biomarkers			Significance
BMI Categories (Kg/m2)	TG (mg/dL)		VLDL (mg/dL)		
	Median	IQR	Median	IQR	
18.5-24.9	116	68.45	23.2	13.69	
25-29.9	184	111.75	36.8	22.35	0.015
≥ 30	194	163.8	38.8	32.76	
Total	160.95	135.5	32.19	27.1	
Variable		Lipid Biomarkers			Significance
Tamoxifen Duration (Months)	TG (mg/dL)		VLDL (mg/dL)		
	Median	IQR	Median	IQR	
3-9	144.5	152.65	28.9	30.53	
10-16	144	101.5	28.8	20.3	
17-23	140	128	28	25.6	0.386
≥24	174	147	34.8	29.4	
Total	160.95	135.5	32.19	27.1	

Table 3. Association of Age Groups, BMI, and Tamoxifen Duration Treatment with TG and VLDL-C in Hormonal BC Women.

Abbreviations, (BMI) Body Mass Index, (TG) Triglycerides, (VLDL-C) Very Low-density Lipoprotein Cholesterol, (IQR) Interquartile Range,(Kg/m^2) Kilograms per Square Meter, (mg/dL) Milligrams per Deciliter.

Discussion

In this cross-sectional study, the impact of tamoxifen as hormonal therapy on lipid profile is examined in the Kurdish women with hormonal positive BC. The levels of TC, HDL-C, and LDL-C were decreased with increasing the age, and the mean levels of TC were statistically significant between different age groups in agreement with the results of comparable study [12] which found the lower level of TC after tamoxifen treatment. In this study, the decreasing in the mean levels of HDL-C were significant when the BMI of the patients were increased, this finding is in contrast to [3] study's results which reported HDL-C level increased after three months of tamoxifen taking. Study of [13] found no changes in HDL-C level. Our study found that the mean levels of TC/HDL-C ratio were significantly increased when the BMI of the patients became higher, but the increasing remained within the reference range for most patients.

Two previous studies [12] and [14] reported a protective effect of tamoxifen therapy against coronary diseases due to the reduction in TC and LDL-C, accompanied by the increase in HDL-C. In a short-term study of [15] which showed statistically positive improvements in 20 postmenopausal women with primary malignant disease, TC and LDL-C were lower in postmenopausal women, but high levels of TG levels were non-significant [16]. Determined the decrease in TC and LDL-C at 3 months, and 6 months of tamoxifen treatment. The peak fall in TC and LDL-C was observed at 6 months, no significant changes happened in TG levels up to 6 months. According to our study, every change happened to TC, HDL-C, LDL-C, TG, VLDL-C, TC/HDL-C, and LDL-C/HDL-C had non-significant differences with increasing the duration of tamoxifen treatment.

The medians of TG and VLDL-C levels were shown a clear increasing in elder patients and in patients with larger BMI, and they were statistically significant. Those changes happened after initiation of the tamoxifen in dyslipidemic patients rather than normolipidic patients due to the fact that tamoxifen may interfere with hepatic lipid metabolism. [17, 18] has shown the similar increasing in both TG and VLDL-C, but the high levels were not statistically significant. In the study of [16], slightly increased happened to TG and VLDL-C levels, but they were not statistically significant. [12] indicated that the TG levels remained unchanged before and after tamoxifen treatment, which is in contrast with our findings. Esteva and Hortobagyi [19] reported that tamoxifen increased the TG levels 12 weeks after initiation of the drug.

According to the studies, tamoxifen may cause negative side effects, including a markedly elevated risk of stroke, pulmonary embolism, and venous thrombosis [20]. Additionally, tamoxifen has been linked to acute pancreatitis brought on by hypertriglyceridemia [21]. Tamoxifen’s potential side effects could be explained by the fact that it is also a partial estrogen agonist, which is linked to a higher risk of endometrial cancer and thromboembolic events [22].

In conclusion, tamoxifen, a hormonal agent used for treating hormone receptor-positive BC, has proven effective in reducing the risk of developing BC in high-risk women. However, its risk-benefit profile must be carefully evaluated for each patient. One of the drug’s effects is its impact on lipid metabolism. In Kurdish women, tamoxifen was found to cause significant changes in lipid levels, particularly as age and BMI increased, specifically, high levels of TG and VLDL-C. Conversely, HDL-C levels were reduced across all BMI categories. Additionally, the TC/HDL-C ratio increased with higher BMI, and TC levels were lowered in elder patients, although within the reference ranges. Healthcare providers should monitor lipid profiles, especially in those with higher BMI or elder age, and recommend lifestyle modifications. Further research is needed for tamoxifen’s long-term effects on lipids.

Acknowledgments

None

Competing Interests

The authors have no competing interests to declare that are relevant to the content of this article.

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