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Serum Lipid Profile and Breast Carcinogenesis among Qatari Young Women

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1. Abstract

This study evaluates the possible association between serum lipids and the incidence of breast cancer (BC) in a control-case survey. The study conducted in Doha included 15 cases newly diagnosed with BC by National Center for Cancer Care & Research (NCCCR) and 30 controls (female students and staff enrolled in Qatar University); 21-55 y. 10 mL of whole blood was collected in EDTA tubes from subjects fasted at least 8 hours. Serum was separated within 1 hour and then samples were stored at -80°C. Lipid profiles (serum TC, HDL, and TG) were analyzed using spectrophotometry. Serum LDL-Cholesterol was calculated using the Friedewald equation. The OR (and 95% CI) was used to ascertain the association between biochemical values and BC for patients and healthy controls, including serum TC, TG, HDL-C, and LDL-C. There are significantly lower values for serum HDL-C and higher for serum TC, LDL-C, and TG in patients compared to healthy controls ($p < 0.05$). The OR and 95% CI using a binary logistic regression model are used to further explore the association between serum lipid parameters and the occurrence of BC. All the biochemical values showed significant differences between the BC patients and healthy controls. TC >5.18 mmol/L, LDL-C >3.36 mmol/L, TG >1.7 mmol/L, and HDL-C <1.00 mmol/L tend to be associated with BC. These findings, although analyzed on a limited number of individuals, seem to indicate an increase in serum lipid parameters and BC in premenopausal women.

2. Introduction

The incidence of all cancer types is still increasing. In 2020, there were 2.3 million women diagnosed with breast cancer (BC) and 685000 deaths globally occurring in the world in women at any age after puberty [1]. However, the death rate attributable to BC continues to decrease following the implementation of detection or screening programs and worldwide improvement of treatments. Many studies have been conducted, with contradicting results, but the relationship between serum lipids and BC incidence remains unclear, and published results have been inconsistent. Laisupasin et al, [2] and Kumar et al, [3] found that plasma triglycerides (TG) were significantly higher in BC patients compared to controls whereas Abu-Bedair et al, [4] and Li et al, [5] reported a significantly lower plasma total cholesterol (TC) in patients with BC compared to controls. Results from observational studies are also controversial, suggesting an association [6-8] or not [9,10] between raised triglycerides and the risk of BC. In addition, a significant increase in serum TG was found in postmenopausal patients with BC, and no significance was found in premenopausal patients when compared with controls [4]. Premenopausal and postmenopausal women with BC have lower [3] or higher [2,5,6] HDL-C levels than healthy females. In addition, LDL-C levels were significantly higher [11] or no significant difference in LDL-C, HDL-C LDL/HDL ratio [10, 12] between control and patients with BC.

While several studies have proposed a possible link between serum

lipids and the incidence of BC, there is no data available among the Qatari population on the relationship between serum lipid levels with cases of BC. The purpose of this study is to investigate the relationships between lipid profiles (serum TG, TC, HDL-C, and LDL-C) and BC in a group of young premenopausal women.

3. Subjects and Methods

To carry out the study, ethical permission was obtained from the Institutional Review Board (IRB) of Qatar University, the Institutional Bio-safety Committee (IBC) of Qatar University, and the Medical Research Center of Hamad Medical Cooperation (HMC). In addition, each participant in the case and control groups signed a consent form as an agreement to participate in this study.

Study population: This epidemiological case-control study included 45 females, with 15 cases matched to 30 controls ranging in age from 21 to 55 years. Case subjects who spoke English or Arabic and lived in the state of Qatar were eligible. The cases were drawn from the National Center for Cancer Care and Research (NCCCR) in Doha. Before admission for BC treatment in NCCCR, no reported history of hyperlipidemia or diabetes mellitus was required for inclusion in the case group. All of the patients had recently been diagnosed with ductal or lobular breast carcinoma. Female students and staff at Qatar University served as the study's controls. The controls were aged ≥ 21 years, had a normal BMI, and had no history of cancer. Exclusion criteria include the use of replacement hormones in the previous 12 months, type 2 diabetes, and illnesses or gallbladder dysfunction; cases and controls were individually matched 1:2 by age (±7 years).

Data collection: Each participant had 10 mL of whole blood drawn, and 4 to 5 mL of blood was collected in two EDTA tubes to preserve the serum. Before sampling, all subjects fasted for at least 8 hours. Serum was separated in 1 hour and samples were stored in a refrigerator at -80ºC.

Data analysis: Serum lipid profiles (TG, TC, and HDL) were analyzed using spectrophotometric kits provided by Stanbio Laboratory. LDL-Cholesterol was calculated using the Friedewald equation (LDL-CHOL = Total CHOL-HDL-CHOL-(TG/5)).

Statistical analysis: To estimate the relationship between lipid profiles and BC, we categorize lipid profiles such as TC, HDL-C, LDL-C, and TG based on clinically abnormal values or cutoff points. The proportion and mean differences between cases and controls were analyzed using the independent t-test.

To estimate the link between BC and serum lipid profiles, odds ratios (OR) and 95% confidence intervals (CI) were calculated, and significant ORs were then examined in a binary logistic regression model. At a p-value < 0.05, all statistical tests in this study are considered significant. The Statistical Package for Social Sciences software was used to analyze the data (SPSS released 20.0, Inc, IBM company).

4. Results and Discussion

As shown in Table 1, the age of all participants (29.04±0.70 y) with a difference between patients and controls (42.0±9.2 vs. 22.6±1.8). Of all patients, 66.7% (10/15) had early-onset BC (age ≤45 years) (Table 1). 100% of the controls were enrolled in Qatar university as students or staff as they completed 12 years of school education, meanwhile, almost 47% of the cases received education after high school. Patients had a higher percentage (33.3%) of reported history of breast or ovarian cancer in a first-degree family member (mother, sister, or aunt). In the reproductive characteristics, there was no significant difference in the age at menarche between the cases and controls. Moreover, the percentage of healthy controls who reported a history of breastfeeding was higher than the patients; however, the mean of the duration of breastfeeding was a little lower in healthy controls compared to patients.

The OR (and 95% CI) was used to ascertain the link between biochemical values and BC for patients and healthy controls, including TC, TG, HDL-C, and LDL-C. There are significantly lower values for HDL-C and higher for TC, LDL-C, and TG in patients compared to healthy controls (Table 3, $p < 0.05$). The OR and 95% CI using a binary logistic regression model are used to further explore the link between lipid parameters and the occurrence of BC as shown in Table 2. All of the biochemical values showed significant differences between the BC patients and healthy controls. The cut-of values TC >5.18 mmol/L, LDL-C >3.36 mmol/L, TG >1.70 mmol/L, and HDL-C <1.00 mmol/L tend to be associated with BC.

In this case-control study of premenopausal women, we detected a direct link between serum lipids and BC. About 87% of the patients are seen to have increased TC ≥ 5.18 mmol/L which is significant OR 0.04 within 95% CI of (0.06-0.28) compared to controls. LDL-C of patients vs. controls is also significant as the increased levels OR is 0.12 with the 95% CI of (0.04-0.34). Similarly, TC levels above the normal range of 1.7 mmol/L included 80% of the patients vs. controls with a significant OR of 7.00 within the 95% confidence interval of 1.94-25.26.

To ensure consistency across statistical tests, we used the independent t-test to compare the significance level of lipid parameters between patients and controls, as shown in Table 3. All lipid parameters (TC, LDL-C, and TG) are considered significant at the 2-tailed test within the 95% CI and p-value <0.01. HDL-C shows significant value also at the 2-tailed test if compared to the 95% CI and $p<0.01$. Therefore, the independent t-test also addresses the significant link between serum lipids and BC among the patients and controls.

There are several possible explanations for the higher lipid parameter plasma concentrations in BC patients. It has been proposed that excessive dietary fat intake is associated with obesity, which is a risk factor for BC in postmenopausal women.

Table 1: Selected characteristics in a breast cancer case-control study.

Variables	Patients (n=15) mean ± SE	Control (n=30) mean ± SE
Age (years)	42.00±9.17	22.57±1.72
Education level (>12 years) %	46.66	100
Family history of BC* (%)	33.33	6.66
Current cigarette smoking (%)	13.33	0
Physical activity (%)	40.1	53.33
Age at menarche (years)	12.64±2.16	12.45±1.24
Age at first pregnancy (years)	16.31±3.70	19.00±3.50
History of breastfeeding (%)	66.7	81.3
Duration of breastfeeding (months)	16.3±14.3	15.4±13.7

*Breast and/or ovarian cancer

Table 2: Odds ratios (OR) and 95% confidence intervals (95% CI) for serum lipid profiles of the patients with breast cancer and controls.

	Controls, n (%)	Patients, n (%)	OR	95% CI
Total cholesterol (mmol/L)				
≥ 5.18	1 (3)	13 (87)	0.04	0.06–0.28
< 5.18	29 (97)	2 (13)	1	
LDL-C (mmol/L)				
≥ 3.36	3 (10)	13 (87)	0.12	0.04–0.34
< 3.36	27 (90)	2 (13)	1	
HDL-C (mmol/L)				
≥ 1.00	30 (100)	7 (47)	2.13	1.25–3.87
< 1.00	0 (0)	8 (53)	1	
Triglycerides (mmol/L)				
≥ 1.7	30 (100)	12 (80)	7	1.94–25.25
< 1.7	0 (0)	2 (13)	1	

HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol

Table 3: Independent t-test for lipid profile in patients and controls

Group		N	Mean	Std. Deviation	Std. Error Mean	sig (2-tailed)	95% CI Lower	95% CI Upper
TC	Control	30	4.4	0.68	0.12	0	-1	-1.85
	Experiment	15	5.8	0.61	0.16	0	-1.01	-1.84
LDL-C	Control	30	2.71	0.57	0.1	0	-0.98	-1.75
	Experiment	15	4.08	0.66	0.17	0.001	-0.95	-1.78
HDL-C	Control	30	1.7	0.76	0.14	0	1.19	0.31
	Experiment	15	0.99	0.18	0.046	0	1.01	0.42
TG	Control	30	0.96	0.27	0.049	0	-1.07	-1.85
	Experiment	15	2.38	1.09	0.28	0	-0.82	-2.04

TC: total cholesterol, HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TG: total triglycerides

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