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Lipid abnormalities in breast cancer of women.

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ABSTRACT

Breast cancer is one of the most prevalent cancers in women with fatal outcome. Associations between lipids, lipoproteins and cancer have been studied by many workers in the past but reports were contradictory and inconclusive. Thus we sought to evaluate lipid abnormalities in breast cancer of women and its link to carcinogenesis. Total 54 untreated breast cancer women and 54 apparently healthy women as control were enrolled. They were investigated for serum triglycerides (TGs), total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL), very low density lipoprotein (VLDL). Cancer stages, age groups and menopausal status were undertaken for the study. In premenopausal patients, serum HDL was found significantly lower but other parameters were not significantly associated. In postmenopausal patients, TC and HDL were significantly lower while serum TGs and VLDL were significantly higher. No change was observed in LDL levels. It is concluded that breast cancer women have characteristic lipid abnormalities in the form of hypertriglyceridemia, raised VLDL and lower HDL levels which may explain their role in carcinogenesis.

KEYWORDS: Breast cancer, lipid abnormalities, carcinogenesis.

Introduction

Breast cancer is the most frequent cancer among women worldwide. There is an association between lipid and breast cancer, because lipids are important to maintain the integrity of cells. In neoplasia, there is rapid and excessive cell proliferation which demands more and more new membrane synthesis. These cells fulfill their high demands of lipids from circulation or by synthesis of new lipids or by degradation of lipoprotein [1]. Various studies have reported an association between lower cholesterol and increased mortality due to cancer [2, 3, 4]. Until now many studies have been done that show conflicting associations between the lipid status and breast cancer. Farid A.A. et al.[5] and V.Michalaki et al.[6] showed that high serum cholesterol was associated with breast cancer while Carter & Feldmen et al.[7] and Lars J. Vatten et al.[8] showed that low serum cholesterol was associated with breast cancer. N.F. Boyd et al.[9], Monica Ferraroni et al.[10] and D.M.Lane et al.[11] showed that high serum HDL-C was associated with breast cancer while I.A.Bani et al.[12],V.Michalaki et a.[6] and E.Kokoglu et al.[13] showed that low serum HDL-C was associated with breast cancer. As the above cited studies were conflicting and inconclusive, the present study was aimed to explore whether there is any association between lipid profile levels and breast cancer.

Materials and Methods

This prospective, observational study was started after prior approval from Institutional Ethics Committee, P. S. Medical College and Shree Krishna Hospital, Karamsad, Gujarat (India). Before enrollment, informed consent was obtained from the patients. 54 patients with histopathologically proven breast cancer between ages 20-84 years and 54 age-matched healthy controls were recruited. Exclusion criteria include Body mass index (BMI) more than 24.9 kg/m2, known case of hyperlipidemia/diabetes mellitus/hypertension/ischemic heart disease, taking drugs that affect lipids and lipoproteins level. The patients of breast cancer and controls were subdivided into (1) premenopausal and postmenopausal patients, (2) ≤50 and > 50 years and (3) different stages of breast cancer according to TNM (Tumour-Node-Metastases) Classification [14]. 5 ml of venous blood samples were collected in plain tubes after an overnight fast. After collection, the samples were allowed to clot for half an hour following which the samples were centrifuged and serum was analysed. Estimation of TGs, TC, and HDL was carried out on fully automated Cobas Integra 400 plus Clinical Chemistry Analyzer using standard colorimetric methods. VLDL and LDL were calculated by using Friedewald's formula [15].

Statistical Analysis

Independent sample-t test was applied to find out the differences between:

(1) All cases and controls ,
(2) Premenopausal breast cancer cases and corresponding controls,
(3) Postmenopausal breast cancer cases and corresponding controls,
(4) Breast cancer patients aged ≤50 years and corresponding controls, and
(5) Breast cancer patients aged >50 years and corresponding controls

ANOVA test has been applied to determine differences between the following groups: (1) Stages of breast cancer and controls , and (2) Stage II and stage III of breast cancer.

Results

Table 1: Characteristics of study population

Characteristics	Number
Females	54
Mean age (years)	45.41
Mean body mass index (kg/m2)	23.3
Menopausal status	
Premenopausal	27
Postmenopausal	27
Stages of the cancer	
Stage I	1
Stage II	22
Stage III	30
Stage IV	1
Age ≤50 years	40
Age >50 years	14

Table 2: Comparison of serum lipids and lipoproteins between different groups of Breast cancer patients and corresponding controls.

Parameters	Groups	N		Controls	Cases	P value
		Cases	Controls			
Total Cholesterol	Premenopausal	27	27	173.06±32.124	164.42±22.90	0.254
	Postmenopausal	27	27	192.64±31.55	172.63±27.34	0.022
	Age 50 years or less	40	40	176.83±34.36	166.13±24.27	0.112
	Age >50 years	14	15	191.53±26.18	175.50±27.11	0.117
	Stage II	22	-	180.84 ± 32.776	174.59±23.00	1
	Stage III	30	-	180.84 ± 32.776	165.20±25.47	0.059
	All patients	54	54	180.84 ± 32.776	168.56±25.121	0.03
Triglyceride	Premenopausal	27	27	94.28±40.063	110.96±33.82	0.097
	Postmenopausal	27	27	101.1±35.35	126±36.82	0.021
	Age 50 years or less	40	40	92.03±37.65	114.63±34.88	0.007
	Age >50 years	14	15	115.80±39.12	130.86±35.92	0.291
	Stage II	22	-	98.51±39.178	109.64±34.18	0.718
	Stage III	30	-	98.51±39.178	126.20±35.79	0.004
	All patients	54	54	98.51±39.178	118.83±35.55	0.005
HDL	Premenopausal	27	27	52.59±10.933	46.58±10.893	0.041
	Postmenopausal	27	27	59.5±14.65	48.85±10.80	0.005
	Age 50 years or less	40	40	54.48±12.28	46.78±10.14	0.003
	Age >50 years	14	15	56.67±15.20	50.57±12.12	0.245
	Stage II	22	-	55.07±13.03	53.00±9.26	1
	Stage III	30	-	55.07±13.03	43.93±10.36	<0.0001
	All patients	54	54	55.07±13.03	47.76±10.702	<0.0001
LDL	Premenopausal	27	27	101.172±25.2600	95.654±19.99	0.369
	Postmenopausal	27	27	112.64±25.62	98.57±24.63	0.057
	Age 50 years or less	40	40	103.54±26.23	96.42±21.33	0.187
	Age >50 years	14	15	111.44±23.65	98.76±24.96	0.171
	Stage II	22	-	105.7±25.584	99.66±19.6	0.954
	Stage III	30	-	105.7±25.584	96.03±23.22	0.23
	All patients	54	54	105.7±25.584	97.03±22.112	0.06
VLDL	Premenopausal	27	27	19.119±8.0400	22.192±6.7643	0.126
	Postmenopausal	27	27	20.22±7.07	25.2±7.36	0.021
	Age 50 years or less	40	40	18.61±7.56	22.92±6.97	0.010
	Age >50 years	14	15	23.16±7.82	26.17±7.18	0.291
	Stage II	22	-	19.85±7.83	21.93±6.84	0.819
	Stage III	30	-	19.85±7.83	25.24±7.16	0.006
	All patients	54	54	19.85±7.83	23.77±7.11	0.01

In postmenopausal patients, mean serum TGs and VLDL levels were found significantly higher ($p<0.05$), TC and HDL levels were found significantly lower ($p<0.05$) than the controls. No change was observed in LDL levels. In premenopausal patients, only HDL levels were found significantly lower ($p<0.05$) than controls. No change was observed in TC, TGs, VLDL and LDL levels.

In older age group (>50 years) of breast cancer patients, no significant changes were found in any of the lipid profile parameters. However serum TC, HDL and LDL were lower and serum TGs and VLDL were higher in cases than controls.

On comparing lipid profile levels of stage II breast cancer patients and controls, no significant change was observed ($p>0.05$). When stage III patients were compared with controls, we found that serum TGs and VLDL were significantly higher and serum HDL was significantly lower than controls ($p<0.05$). Overall, when patients (n=54) were compared with controls (n=54) serum TC, HDL were significantly lower ($p<0.05$) while serum TGs and VLDL were significantly higher ($p<0.05$) than controls. No change was observed in LDL levels than controls.

Discussion

The human mammary glands metabolize lipids from plasma which is under the control of gonadal hormones. These sex hormones need cholesterol as precursor substance for biosynthesis. During rapid and excess proliferatin of cells as encountered in malignancies, there is a high demand of lipids for newer membrane synthesis and maintaining cellular integrity. These requirements of lipids are fulfilled from circulating blood lipids, synthesis of new lipids or by degradation of various lipoproteins (LDL, VLDL, HDL). Kokoglu et al.[13] and Fiorenza et al.[16] found that breast cancer patients had significantly lower serum TC, HDL and higher serum triglyceride and VLDL than controls. These results were in agreement with our study. Monica Ferraroni et al.[10] and Feldmen EB et al.[7] found significantly lower total cholesterol and LDL-C in breast cancer patients than controls which was in agreement with the current study.However,higher serum HDL was showed by Monica Ferraroni et al.[10] in breast cancer patients, although not significant.

Kokoglu et al. [13] have also found decrease serum TC ($p<0.05$) and HDL ($p<0.05$) while significant increase in serum TGs ($p<0.05$) were noticed in postmenopausal patients as compared to the corresponding controls. These findings were consistent with our study. They also noticed that changes in serum lipids were pronounced with advance in cancer stages which is similar to what was observed in our study also.

The reduction in serum total cholesterol with increasing stage of disease can be partly attributed to a reduction in HDL or high LDL receptor activity. Lower level of LDL in our study may be because of low cholesterol. New membrane synthesis by rapidly dividing breast cancer cells might consume serum lipid (cholesterol) which accounted for its lower values in cancerous patients. Lipids (cholesterol) are primarily required by gonads to synthesize sex hormones and gametogenesis. Elevated estradiol secretion could influence the abnormal growth in mammary glands and lymphoid system. Excess biosynthesis of estradiol may utilize serum cholesterol, leading to hypocholesterolemia [17]. Hypertriglyceridemia may be due to decreased activity of lipoprotein lipase in white adipose tissues in cancer cases, resulting in impaired catabolism of serum triglyceride and increased serum triglyceride levels [19, 20]. Elevated levels of triglycerides are associated with a decreased level of sex-hormone-binding globulins, resulting in increased amounts of free estradiol and increased breast cancer risk [18]. Low lipid level may be the early marker of neoplasia. The mechanism responsible for this defect in lipid metabolism has not been clearly understood.

Conclusion

We concluded that breast cancer women have characteristic lipid abnormalities in the form of hypertriglyceridemia, raised VLDL and lower TC, HDL levels. These alterations of serum lipid and lipoproteins could suggest their involvement as risk factor for developing breast cancer.

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