ALTERATIONS OF SERUM CHOLESTEROL AND SERUM LIPOPROTEIN IN BREAST CANCER OF WOMEN

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ABSTRACT

Fasting blood sample of 50 normal subjects (control) and 100 patients of breast cancer were investigated for serum total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol, very low density lipoprotein, high density lipoprotein cholesterol:low density lipoprotein cholesterol ratio and total cholesterol:high density lipoprotein cholesterol ratio during breast cancer of women. Five cancer stages, types, age groups, parity and menopausal status were undertaken for the study. It was observed that there was a significant rise in serum total cholesterol and low density lipoprotein cholesterol whereas high density lipoprotein cholesterol and very low density lipoprotein cholesterol were not significant. The ratio of high density lipoprotein cholesterol:low density lipoprotein cholesterol and total cholesterol:high density lipoprotein cholesterol values increased significantly in breast cancer patients.

KEY WORDS

Breast cancer, cholesterol, lipoprotein profile

INTRODUCTION

Plasma lipids level reflects dietary lipid intake in individual. There are several reports of elevated plasma lipid level such as total lipids (TL), phospholipids (PL), triglycerides (TG), total cholesterol (T-C), low density lipoprotein (LDL-C) and free fatty acids (FFA) in pre and post menopausal breast cancer patients (1,2,3). It has been postulated that changes in the concentration of serum lipids in the breast cancer patients could result in increase production of tumor necrosis factor and inhibit adipose lipoprotein lipase activity by the action of insulin (2,4). These changes impair the catabolism of very low density lipoprotein (VLDL), leading to an increase in high density lipoproteins cholesterol (HDL-C). Epidemiology studies reveal that HDL-C and breast cancer are influenced by variables like dietary fat intake, alcohol consumption, weight, country of residence, pregnancy, endogenous hormones, smoking, exercise and socioeconomic status (5). HDL-C level has been shown to be higher in subject with mammography dysphasia and family history of breast cancer (6,7). They have, however, reported either elevated or depressed level of HDL-C in women with breast cancer.

Thus HDL-C level alone, at present, cannot be taken into consideration as a causative factor. It was found that patients with more advanced breast cancer have significantly lower concentration of HDL-C than do patients with less advanced disease (2). Few studies have, however, directly addressed the relationship of HDL-C with breast cancer. But a relationship of HDL-C to breast cancer is still a subject of controversy (8). Plasma T-C and LDL-C, were found to be significantly elevated whereas HDL-C was significantly decreased in breast cancer patients. These studies suggests that higher level of T-C may play important role in carcinogenesis (9). Serum lipoprotein profile in patients with cancer and non cancer subjects in which T-C, LDL-C, HDL-C, were analyzed in 530 cancer patients out of which 32 were of breast cancer patients. Conflicting results have been reported on LDL-C, HDL-C and TG level in different types of tumors. The highest values of T-C, HDL-C, LDL-C were recorded in breast cancer patients (10). An association between overweight and a high fat diet and incidence of breast and uterus cancer has been suggested with no convincing evidence. (11). Present work is an attempt to determine the alterations in serum cholesterol and lipoprotein due to breast cancer in women and their probable role in carcinogenesis.

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MATERIALS AND METHODS

Serum was obtained from 50 normal healthy persons (control) and 100 untreated breast cancer patients with clinical and histopathological evidence, under aseptic conditions. Fasting venous blood was drawn and

serum was separated and analyzed within 6 hours after its separation. The following parameters were analyzed with each sample. (i) T-C (ii) HDL-C (iii) LDL-C, (iv) VLDL, (v) HDL: LDL ratio and (vi) T-C: HDL ratio.

The investigations were done by the method of Wybenga *et al.* (1970). The estimations were done using ready made kits. The comparative study was carried out in 5 groups viz - (a) different stages; (b) different types; (c) Parity (number of children) of breast cancer patients; (d) Age factor of breast cancer patient and (e) pre and postmenopausal state of breast cancer patients. Full attention was given to quality control.

Data thus obtained was analyzed by using student t-test by statistical packages for social science software (SPSS). Statistical analysis where the value of $p < 0.05$ considered as significant and $p < 0.01$ as highly significant.

RESULTS

The results under five groups, are presented in tables I to V.

Table - I : Shows the mean values of serum T-C, HDL-C, LDL-C, VLDL (lipoprotein profile), HDL:LDL ratio and T-C:HDL-C ratio during different stages of breast cancer. Value of T-C was very high in all the four stages of breast cancer and was highly significant. The values of HDL-C and VLDL of control group when compared with different stages of breast cancer was found to be non-significant. LDL value was highly significant in experimental group. However, ratio of HDL:LDL was also highly significant. Similarly, ratio of T-C:HDL was also highly significant.

Table - II : Shows the mean value of serum T-C, HDL-C, LDL-C, VLDL (lipoprotein profile), HDL:LDL ratio

TABLE I. SERUM CHOLESTREROL AND LIPOPROTEINS VALUES DURING DIFFERENT STAGES OF BREAST CANCER. (VALUES ARE MEAN AND $\pm$ SEM)

PARAMENTERS	NORMAL RANGE	CONTROL	STAGE I	STAGE II	STAGE III	STAGE IV
T-C (mg/ml)	130-250	179.22 $\pm$ 2.75	284.48 $\pm$ 7.29**	274.39 $\pm$ 4.01**	288.63 $\pm$ 3.09**	284.31 $\pm$ 6.32**
HDL-C(mg/dl)	35-75	55.98 $\pm$ 0.82	55.85 $\pm$ 1.98	57.27 $\pm$ 1.22	55.82 $\pm$ 1.01	55.72 $\pm$ 2.13
LDL-C (mg/dl)	50-140	88.33 $\pm$ 2.22	193.85 $\pm$ 6.33**	184.69 $\pm$ 3.83**	195.80 $\pm$ 3.01**	189.24 $\pm$ 6.78**
VLDL(mg/dl)	Upto 40	35.19 $\pm$ 0.52	34.83 $\pm$ 2.52	32.41 $\pm$ 0.56	37.01 $\pm$ 0.91	38.68 $\pm$ 2.47*
HDL:LDL	1:2	1:1.60 $\pm$ 1:0.16	1:3.47 $\pm$ 0.21**	1:3.26 $\pm$ 1:0.34**	1:3.57 $\pm$ 1:0.15**	1:3.48 $\pm$ 1:0.21**
T-C:HDLRATIO	<4.5:1	3.20 $\pm$ 0.15:1	5.13:1 $\pm$ 0.18:1**	4.86:1 $\pm$ 0.15:1**	5.27:1 $\pm$ 0.15:1**	5.26:1 $\pm$ 0.22:1**

** highly significant at 95% level (P<.001)
*Significant at 95% level (P<.005)

TABLE II. SERUM CHOLESTEROL AND LIPOPROTEIN VALUES DURING DIFFERENT TYPES OF BREAST CANCER. (VALUES ARE MEAN AND $\pm$ SEM).

PARAMETERS	NORMAL RANGE	CONTROL	DUCTAL	INTRADUCTAL	INFILTRATING DUCTAL
T-C(mg/ml)	130-250	179.22 $\pm$ 2.75	287.51 $\pm$ 3.20**	282.73 $\pm$ 3.36**	280.28 $\pm$ 8.03**
HDL-C(mg/dl)	35-75	55.98 $\pm$ 0.82	55.90 $\pm$ 1.36	56.51 $\pm$ 0.85	55.06 $\pm$ 2.11
LDL-C(mg/dl)	50-140	88.33 $\pm$ 2.22	193.64 $\pm$ 3.65**	191.73 $\pm$ 2.78**	187.75 $\pm$ 7.56**
VLDL(mg/dl)	Upto 40	35.19 $\pm$ 0.52	37.75 $\pm$ 1.44	32.47 $\pm$ 0.60	37.47 $\pm$ 1.08
HDL:LDL	1:2	1:1.60 $\pm$ 1:06	1:3.57 $\pm$ 1:1.15**	1:3.41 $\pm$ 1:0.14**	1:3.44 $\pm$ 1:0.24**
T-C:HDLRATIO	<4.5:1	3.20 $\pm$ 0.15:1	5.13:1 $\pm$ 0.15:1**	4.86:1 $\pm$ 0.13:1**	5.16:1 $\pm$ 0.28:1**

**highly significant at 95% level (<.001)
*Significant at 95% level (<.005)

and T-C:HDL-C ratio in normal (control) and breast cancer patients of different types. The T-C value was very high and highest in ductal carcinoma than in intraductal and infiltrating ductal carcinoma. Overall,

the values were highly significant. The value of HDL-C and VLDL was non significant. LDL-C value was high in all types of breast cancer and was highly significant.

TABLE III. SERUM CHOLESTEROL AND LIPOPROTEINS VALUES RELATED TO PARITY AND BREAST CANCER PATIENTS.

(VALUES ARE MEAN AND $\pm$ SEM)

PARAMETERS	NORMAL RANGE	CONTROL	PARITY – 1	PARITY-2-5
T-C (cm/ml)	130-250	179.22 $\pm$ 2.75	278.87 $\pm$ 5.03**	285.29 $\pm$ 2.33**
HDL-C (mg/dl)	35-75	55.98 $\pm$ 0.82	52.57 $\pm$ 3.44	56.15 $\pm$ 0.72
LDL-C(mg/dl)	50-140	88.33 $\pm$ 2.22	191.85 $\pm$ 3.65**	192.50 $\pm$ 2.27**
VLDL(mg/dl)	Upto 40	35.19 $\pm$ 0.52	34.40 $\pm$ 3.69	36.15 $\pm$ 0.67
HDL:LDL	1:2	1:1.60 $\pm$ 1:06	1:3.74 $\pm$ 1:0.36**	1:3.48 $\pm$ 1:0.14**
T-C:HDLRATIO	<4.5:1	3.20 $\pm$ 0.15:1	5.41:1 $\pm$ 0.40:1**	5.14:1 $\pm$ 0.13:1**

PARITY = Number of Children.
 **highly significant at 95% level (p<.001)
 Significant at 95% level(p<.005)

TABLE NO. IV: SERUM CHOLESTEROL AND LIPOPROTEINS VALUES IN RELATION TO AGE GROUP OF BREAST CANCER PATIENTS.

(VALUES ARE MEAN AND $\pm$ SEM)

PARAMETERS	NORMAL RANGE	CONTROL	>31 YEARS	<30 TO>51 YEARS	<51 YEARS
T-C(mg/ml)	130-250	179.22 $\pm$ 2.75	286.67 $\pm$ 4.84**	285.61 $\pm$ 2.88**	279.85 $\pm$ 4.94**
HDL-C(mg/dl)	35-75	55.98 $\pm$ 0.82	54.97 $\pm$ 1.59	56.32 $\pm$ 0.88	55.71 $\pm$ 1.92
LDL-C(mg/dl)	50-140	88.33 $\pm$ 2.22	195.86 $\pm$ 5.53**	192.27 $\pm$ 2.70**	188.78 $\pm$ 4.20**
VLDL(mg/dl)	Upto 40	35.19 $\pm$ 0.52	35.76 $\pm$ 1.66	36.32 $\pm$ 0.84	35.32 $\pm$ 1.34
HDL:LDL	1:2	1:1.60 $\pm$ 1:06	1:3.59 $\pm$ 1:0.19**	1:3.48 $\pm$ 1:0.13**	1:3.44 $\pm$ 1:0.16**
T-C:HDLRATIO	<4.5:1	3.20 $\pm$ 0.15:1	5.23:1 $\pm$ 0.21:1**	5.14:1 $\pm$ 0.16:1**	5.09:1 $\pm$ 0.14:1**

**highly significant at 95% level (p<.001)
 *Significant at 95% level (p<.005)

TABLE NO. V. SERUM CHOLESTEROL AND LIPOPROTEINS VALUES DURING PRE AND POSTMENOPAUSAL STATUS OF BREAST CANCER PATIENTS.

(VALUES ARE MEAN AND $\pm$ SEM)

PRAMETERS	NORMAL RANGE	CONTROL	PREMENOPAUSAL	POSTMENOPAUSAL
T-C(mg/ml)	130-250	179.22 $\pm$ 2.75	283.09 $\pm$ 4.38**	285.12 $\pm$ 2.53**
HDL-C(mg/dl)	35-75	55.98 $\pm$ 0.82	56.88 $\pm$ 0.94	55.74 $\pm$ 0.98
LDL-C(mg/dl)	50-140	88.33 $\pm$ 2.22	191.09 $\pm$ 3.96**	192.79 $\pm$ 2.61**
VLDL(mg/dl)	Upto 40	35.19 $\pm$ 0.52	35.14 $\pm$ 0.86	36.49 $\pm$ 0.93
HDL:LDL	1:2	1:1.60 $\pm$ 1:06	1:3.37 $\pm$ 1:0.12**	1:3.54 $\pm$ 1:1.042**
T-C:HDLRATIO	<4.5:1	3.20 $\pm$ 0.15:1	5.03:1 $\pm$ 1:0.14**	5.24:1 $\pm$ 0.12:1**

**highly significant at 95% level (p<.001)
 *Significant at 95% level (p<.005)

Ratio of HDL:LDL was also highly significant. Similarly the ratio of T-C:HDL-C was also found to be highly significant in all the types.

TABLE III : Shows the mean values of serum T-C, HDL-C, LDL-C, VLDL (lipoprotein profile), HDL:LDL ratio and T-C:HDL-C ratio in relation to parity in breast cancer patients. In all parity, one and two to five, total cholesterol was found to be high in cancer patients and the value was highly significant. The values of HDL-C and VLDL were not much different from control and were non-significant, whereas the value of LDL-C was very high and highly significant. The ratio of HDL:LDL and T-C:HDL-C in all parity of breast cancer patients was highly significant.

TABLE IV : Shows the value of serum T-C, HDL-C, LDL-C, VLDL (lipoprotein profile), HDL:DL ratio, T-C, HDL-ratio in relation to age group of cancer patients. In all the groups the T-C was highly significant, whereas HDL-C was non-significant. In experimental group LDL-C value was very highly significant. The ratio of HDL:LDL and T-C:HDL in experimental group was very high and highly significant.

TABLE V : Shows the mean value of serum T-C, HDL-C, LDL-C, VLDL (lipoprotein profile), HDL:LDL ratio, T-C:HDL-C ratio in premenopausal and postmenopausal stage of breast cancer patients. The value of total cholesterol when compared with premenopausal and postmenopausal, were higher in patient with postmenopausal than premenopausal, but in both state values were highly significant. There was no significant different in the values of HDL-C and VLDL in both cases. The value of LDL-C was higher in pre and postmenopausal state of breast cancer patient and was highly significant. HDL:LDL ratio was high in experimental group and was highly significant. The ratio of T-C:HDL-C was also highly significant.

DISCUSSION

Human mammary tissue metabolizes lipids from plasma affected by female gonadal hormones. Malignant proliferation of breast tissue in women has been associated with changes in plasma lipid and lipoproteins levels (13). In the present studies elevated level of total cholesterol has been observed in different stages of breast cancer patients but it was not related with the advancing stages. Overall elevated total cholesterol was highly significant in breast cancer of women than control group, as also reported by Mady (2000) and Ray *et al.* (2001) (14,15). HDL-C level was not significant in the present case but was noted to be significantly decreased in breast cancer patients. Contrary to this HDL-C level have been shown to be higher in subject with mammographic dysplasia and family history of breast cancer (9). Present observation indicate that patients with more advanced breast

cancer have significantly lower concentration of HDL-C than do patients with less advanced disease. Few studies have, however directly shown the relationship of HDL-C to breast cancer, but still is a subject of controversy (8). Studies with different stages of breast cancer show that HDL-C and VLDL levels were not significant. However, VLDL was significant in stage IV patients only in the present case. The data from healthy females indicate that overall VLDL and HDLC levels were, in general, within range. However, slight decrease in T-C, HDL-C and LDL-C levels were observed in patients at stage IV only. No significant differences were found in HDL-C and LDL-C levels between stage I and healthy control as also found by Kokulu *et al.* (1994).

The relationship between T-C and LDL-C in breast cancer patients was observed during present studies, as also reported by Hoyer and Engholon (1992) (17). Our studies indicate significant increase in T-C and LDL-C levels. Non significant level of HDL-C and high level of T-C also affect the ratio of T-C:HDL-C. The high level of LDL-C also affect the ratio of HDL:LDL, however, the ratio of T-C:HDL-C and the ratio of HDL:LDL was highly significant. The increased T-C and LDL-C values and decreased HDL-C value increases the risk of coronary heart disease (22). This shows that the uptake of cholesterol from the cancer cells can be a risk factor in breast cancer of different types. There is an apparent association between T-C level and breast cancer at different types. Elevated T-C and LDL-C values were found in all three types of breast cancer, ductal, intraductal and infiltrating ductal carcinoma. The values were higher in ductal as compared to intraductal and infiltrating carcinoma. Elkhadrawy, *et al* (1998) reported conflicting results. He concluded that there is no apparent association between the T-C and the breast (ductal) carcinoma, contrary to the present findings.

Parity and age at first child birth are other factors that influence breast cancer risk. Women whose full term pregnancy occurs after the age of 30 have two to five fold increase in breast cancer risk compared with women having full term pregnancy at 18-19 years of age (19). Our studies indicate that T-C and LDL-C were highly significant in all parity cases. HDL-C and VLDL were not significant whereas the ratio of HDL-C, LDL-C and T-C:HDL-C were highly significant. In different age groups, T-C and LDL-C were highly significant and HDL-C and VLDL-C were not significant but the ratio of T-C:HDL-C and HDL-C:LDL-C were highly significant. No correlation was found between T-C level and breast cancer survival in all the age groups during present studies. The T-C level was higher in the age group > 31 years as compared to other. However, in the age group < 51 years T-C and LDL-C level decreased. This may be attributed to increased age factor. The observation are in accordance with report of Tornberg *et al.* (1988).

Serum T-C was highly significant and increased in pre and postmenopausal state. The values were higher in postmenopausal cases as compared to premenopausal case. However, decreased HDL-C was observed in patients with breast cancer in both states. It is reported that association between lipoprotein alteration is independent of menopausal status (14,21). Contrary to this present studies reveal that there is an association between lipoprotein alteration and menopausal status. The ratios between HDL-C: LDL-C and T-C:HDL-C were highly significant. This significance was more seen in postmenopausal cases. Thus it is likely that postmenopausal women are more prone to breast cancer.

Present studies show that T-C and LDL-C levels were high in all parameters investigated. Thus it can be stated that the high levels of total cholesterol and LDL-C may play a significant role in carcinogenesis of breast of women in India.

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