Plasma lipid profile in gynecologic cancers

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Summary

Background: Lipids are associated with cancer because they play a key role in the maintenance of cell integrity. We studied the relationship of plasma lipids with gynecologic cancer. *Methods:* A total of 196 female individuals were included in the study. Of these 50 were normal subjects. The remaining were cancer patients: 80 breast cancer, 40 ovarian cancer and 26 patients with other gynecologic cancers. Plasma levels of triglycerides, total cholesterol, LDL-cholesterol and HDL-cholesterol were estimated by using spectrophotometer. *Results:* In breast cancer patients there is moderate increase in the plasma levels of triglycerides (18%) and cholesterol (21%), and a high increase in LDL-cholesterol (43%), while there is a moderate decrease in HDL-cholesterol levels (30%) when compared with normal subjects. In ovarian cancer patients, there is a high decrease in the plasma levels of triglycerides (31%) and HDL-cholesterol (39%), while a moderate decrease in cholesterol (28%) and LDL-cholesterol levels (11%) when compared with normal subjects. In gynecologic cancers other than breast and ovarian cancer, there is a moderate decrease in plasma levels of the triglycerides (25%), cholesterol (21%), and HDL-cholesterol levels (27%), while a non-significant decrease in LDL-cholesterol (6.2%) when compared with normal subjects. *Conclusions:* Plasma lipid levels, except HDL-cholesterol, are raised in breast cancer and are decreased in other gynecologic cancers. HDL-cholesterol is decreased in all gynecologic cancers. As there is an alteration in the plasma lipid profile during gynecologic cancers, it may be helpful for diagnosis of the disease.

Key words: Plasma lipids; Gynecologic cancers.

Introduction

Breast cancer and ovarian cancer are the major gynecologic cancers [1]. Lipids are carried in body fluids with the help of lipoproteins [2, 3]. Chylomicrons transport triglycerides from the intestine to all cells. Very low density lipoproteins (VLDL) are involved in the transportation of triglycerides from the liver to other cells. Low density lipoproteins (LDL) are responsible for the transport of cholesterol from the liver to the cells and high density lipoproteins (HDL) are involved in the transport of cholesterol from cells to the liver. Chylomicrons and very low density lipoproteins are rapidly catabolized [4, 5]. Thus triglycerides, cholesterol, LDL-cholesterol and HDL-cholesterol constitute the plasma lipid profile.

Researchers have reported an association of plasma/serum lipids and lipoproteins with different cancers. As neoplastic disease is related to new growth, there is a greater utilization of lipids including total cholesterol, lipoproteins, and triglycerides for new membrane biogenesis. Cells fulfill these requirements either from circulation, by synthesis through the metabolism or from degradation of major lipoprotein fractions like VLDL, LDL or HDL. The plasma concentrations of lipids are not the single additive function of intake, utilization and biosynthesis because of the continuous cycling in and out of the blood stream [6]. Our study was designed to evaluate the relationship between the plasma lipid profile (triglycerides, cholesterol, LDL-cholesterol and HDL-cholesterol) and gynecologic cancers.

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Materials and Methods

Subjects

A prospective study was carried out on 196 women. Of these, 50 were normal subjects who had no complaint nor any major illness in the last few years. They were close relatives of the patients who were hospitalized. The remaining subjects were cancer patients: 80 breast cancer, 40 ovarian cancer and 26 patients with other gynecologic cancers. No patient had a history of thyroid disease, diabetes or any other major illness that could affect lipid metabolism. The patients were not treated with any chemotherapy, radiation or surgery before the sample collection.

Fasting blood samples were collected from the Combined Military Hospital, Rawalpindi, Pakistan and NORI Hospital, Islamabad, Pakistan. The plasma was stored at -20°C until used for estimation of the plasma lipid profile.

Estimation of plasma lipid profile

Plasma levels of triglycerides, total cholesterol, LDL-cholesterol and HDL-cholesterol were estimated by using a spectrophotometer.

Triglycerides

Triglycerides were determined by an enzymatic method (GPO-PAP method) using the commercially available kit manufactured by Human, Germany.

Procedure

Three cuvettes were washed with distilled water and labelled blank, standard and sample; 20 ml of distilled water, 20 ml of standard, and 20 ml of sample were pipetted into each cuvette, respectively. Chromogen reagent (2 ml) was added to each cuvette. Contents of all the cuvettes were mixed thoroughly and incubated for five minutes at room temperature. The wavelength of the spectrophotometer was set at 500 nm and after some time the results were displayed. Blood triglyceride levels were calculated by applying the following formula.

$$\text{Triglycerides mg/dl} = \frac{\text{Absorbance of sample}}{\text{Absorbance of standard}} \times 200$$

Total cholesterol

Rapid enzymatic determination of the total cholesterol by the CHOD-PAP method [7] was performed using the commercially available kit (Human, Germany).

Procedure

Three cuvettes were washed with distilled water and labelled blank, standard or sample; 20 ml of distilled water, 20 ml of standard, and 20 ml of sample were pipetted into each cuvette, respectively. Chromogen reagent (2 ml) was added to each cuvette. Contents of all the cuvettes were mixed thoroughly and incubated for five minutes at 37°C. The wavelength of the spectrophotometer was set at 500 nm and after some time the results were displayed. Blood cholesterol levels were calculated by applying the following formula.

$$\text{Cholesterol mg/dl} = \frac{\text{Absorbance of sample}}{\text{Absorbance of standard}} \times 200$$

LDL-cholesterol

LDL-cholesterol was determined by the precipitation method. Tests were performed by using the commercially available kit manufactured by Randox, Germany.

Procedure

For sample preparation 100 ml of sample and 1000 ml of precipitant were placed in a tube. After thorough mixing, the tube was allowed to stand for 15 min at room temperature and then was centrifuged at 1500 rpm for 15 min. Supernatant was separated from the sediment and cholesterol was measured by the CHOD-PAP method. LDL-cholesterol levels were calculated by applying the following formula.

LDL-cholesterol mg/dl = Total cholesterol – Cholesterol in supernatant.

HDL-cholesterol

HDL-cholesterol was determined by using the commercially available kit (Randox, Germany).

Procedure

For sample preparation 200 ml of sample and 500 ml of precipitant were placed into a tube. After through mixing, the tube was allowed to stand for ten minutes at room temperature and then was centrifuged at 4000 rpm for ten minutes. Supernatant was separated from the sediment and cholesterol was measured by the CHOD-PAP method.

Statistical Analysis

The computer program SPSS 11.0 version was used for statistical analyses. The Student's t-test was performed to compare mean values of the parameters; p value < 0.05 was considered as statistically significant.

Results

In the present study plasma levels of triglycerides in control subjects ranged from 120-189 mg/dl (mean 158.29 ± 6.31), plasma levels of cholesterol ranged from 133-206 mg/dl (mean 176.35 ± 7.62), plasma levels of LDL-cholesterol ranged from 48-93 mg/dl (mean 76.87 ± 5.05) and plasma levels of HDL-cholesterol ranged from 41-73 mg/dl (mean value 54.42 ± 4.73) (Table 1).

Table 1. — *Plasma lipid profile of control subjects and patients with gynecologic cancers (mean ± SD).*

	Triglycerides (mg/dl)	Cholesterol (mg/dl)	LDL-cholesterol (mg/dl)	HDL-cholesterol (mg/dl)
Control subjects	158.29 ± 6.31	176.35 ± 7.62	76.87 ± 5.05	54.42 ± 4.73
Breast cancer	186.44** ± 5.61	214.13** ± 6.23	109.99** ± 4.12	38.22** ± 3.31
Ovarian cancer	109.13 ± 8.45**	127.77 ± 8.09**	68.55* ± 8.01	33.33 ± 7.54**
Other gynecologic cancers	118.23 ± 7.19*	138.97 ± 5.81*	66.12* ± 6.41	40.00 ± 3.03**

* $p < 0.01$ as compared to control group; ** $p < 0.05$ as compared to control group.

In patients with breast cancer plasma levels of triglycerides ranged from 143-218 mg/dl (mean 186.44 ± 5.61), plasma levels of cholesterol ranged from 176-243 mg/dl (mean 214.13 ± 6.23), plasma levels of LDL-cholesterol ranged from 83-172 mg/dl (mean 109.99 ± 4.12), and plasma levels of HDL-cholesterol ranged from 26-63 mg/dl (mean 38.22 ± 3.31). For breast cancer patients there was a moderate increase in plasma levels of triglycerides (18%) and cholesterol (21%), and a high increase in LDL-cholesterol (43%) while there was a moderate decrease in HDL-cholesterol levels (30%) when compared with normal subjects.

In patients with ovarian cancer plasma levels of triglycerides ranged from 45-178 mg/dl (mean 109.13 ± 8.45), plasma levels of cholesterol ranged from 39-241 mg/dl (mean 127.77 ± 8.09), plasma levels of LDL-cholesterol ranged from 17-116 mg/dl (mean 68.55 ± 8.01), and plasma levels of HDL-cholesterol ranged from 13-59 mg/dl (mean 33.33 ± 7.54) (Table 1). For ovarian cancer patients there was a high decrease in plasma levels of triglycerides (31%) and HDL-cholesterol (39%), while a moderate decrease in cholesterol (28%) and LDL-cholesterol levels (11%) when compared with normal subjects.

In patients with cancers other than breast and ovarian, the plasma levels of triglycerides ranged from 46-178 mg/dl (mean 118.23 ± 7.19), plasma levels of cholesterol ranged from 39-245 mg/dl (mean 138.97 ± 5.81), plasma levels of LDL-cholesterol ranged from 29-92 mg/dl (mean 66.12 ± 6.41) and plasma levels of HDL-cholesterol ranged from 32-64 mg/dl (mean 40.00 ± 3.03) (Table 1). For gynecologic cancers other than breast and ovarian, there was a moderate decrease in the plasma levels of triglycerides (25%), cholesterol (21%), and HDL-cholesterol (27%) while a non-significant decrease in LDL-cholesterol (6.2%) when compared with normal subjects.

Discussion

Several studies of plasma lipid alterations in animals with neoplasms have been conducted [8-10]. In the past few years there have been reports related to general

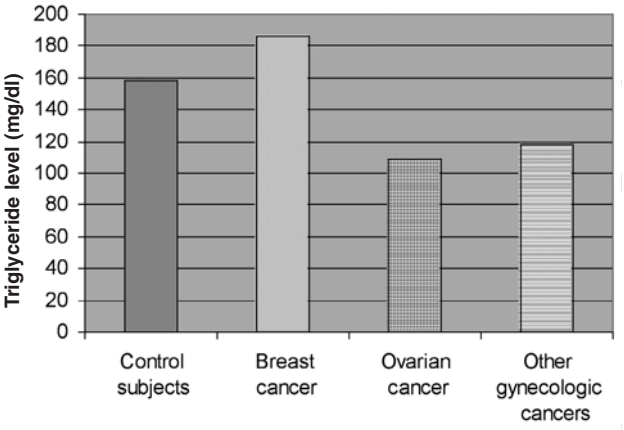

Figure 1. — Plasma triglyceride levels of control subjects and gynecologic cancer cases.

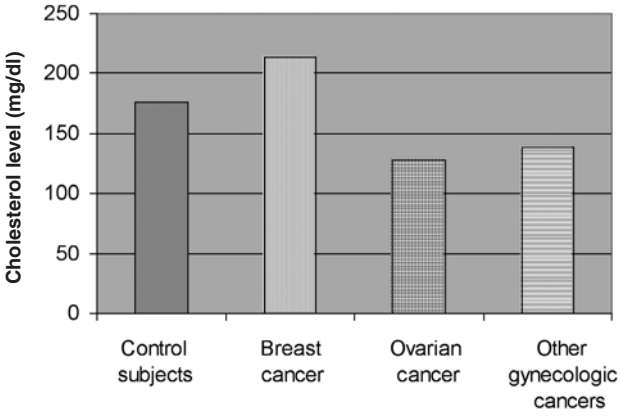

Figure 2. — Plasma cholesterol levels of control subjects and gynecologic cancer cases.

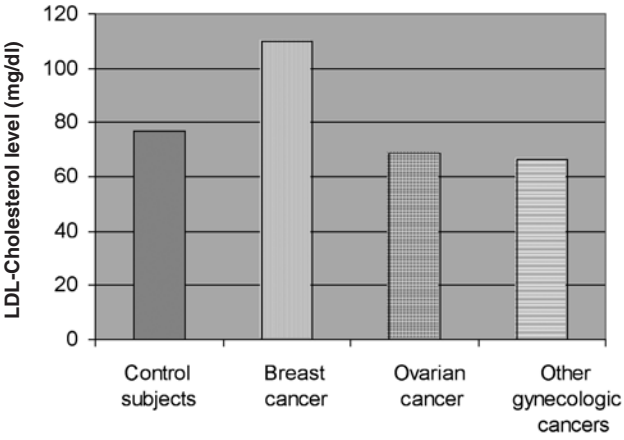

Figure 3. — Plasma LDL-cholesterol levels of control subjects and gynecologic cancer cases.

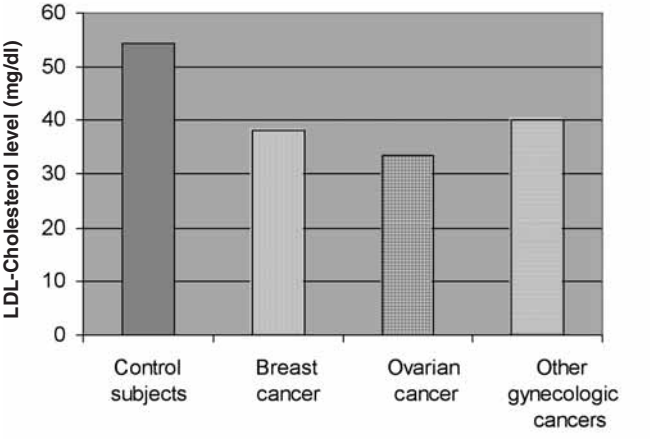

Figure 4. — Plasma HDL-cholesterol levels of control subjects and gynecologic cancer cases.

cancer, hematological cancers, and head and neck cancer [11, 12, 6], The return of plasma lipids and lipoproteins towards normal limits during remission in leukemia patients confirms the correlation of lipid alterations with primary disease activity [12, 13].

In the present study, plasma triglycerides, cholesterol and LDL-cholesterol showed a highly significant ($p < 0.01$) increase in breast cancer patients when compared with normal control subjects, while HDL-cholesterol levels showed a highly significant ($p < 0.01$) decrease. In ovarian cancer all the plasma lipid components showed a highly significant ($p < 0.01$) decrease except for LDL-cholesterol which was significantly decreased ($p < 0.05$). In gynecologic cancers other than breast and ovarian cancer, all the plasma lipid components showed a significant ($p < 0.05$) decrease except for HDL-cholesterol which was highly significantly decreased ($p < 0.01$).

The pathophysiologic mechanism implicated in plasma lipid alterations during neoplasm has not been determined. Lipids are major cell membrane components essential for various biological functions including cell growth and division of normal and malignant tissues. Low levels of cholesterol in the proliferating tissues and in blood compartments could be due to the process of carcinogenesis. The raised plasma concentrations of these parameters in patients with breast cancer may be due to an increased rate of lipid absorption as the fat-splitting enzymes, lipases, were also found to be increased in the patients [15].

Briefly we conclude that plasma lipid levels, except HDL-cholesterol, are raised in breast cancer and are decreased in other gynecologic cancers. HDL-cholesterol is decreased in all gynecologic cancers. As there is an alteration in the plasma lipid profile during gynecologic cancers, this profile may be helpful for diagnosis of the disease.

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