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Association between Lipid Profile and Ovarian Cancer in women of North India

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Abstract

Objective: The aim of this study was to compare serum lipid profiles: total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-c), low density lipoprotein cholesterol (LDL-c) and very low density lipoprotein cholesterol (VLDL-c) and lipid ratio among ovarian cancer (OC) patients and healthy controls.

Methods: Total 300 subjects were enrolled in this study. Study group comprised of 150 clinically and histologically proved cases of ovarian carcinoma and 150 healthy women recruited as a control group. Plasma levels of TC, TG and HDL were determined using a commercially available kit and a semi-automated analyzer. LDL and VLDL were calculated by Friedewald's formula.

Results: In our study, we found the higher level of mean serum cholesterol, TGs, LDL-c and VLDL in OC patients as compared to the controls. The HDL level is higher in controls as compared to study group. TGs, HDL-c VLDL were found highly significant in OC patients as compared to controls. The Ratio of TC/HDL, LDL/HDL, HDL/LDL was also found significantly higher in OC patients as compared to controls.

Conclusions: The results of the present study shows that plasma lipid levels, except HDL-cholesterol, are increase in OC. As there is an alteration in the plasma lipid profile during gynecologic cancers, it may be helpful for diagnosis of the disease. Further studies needed to investigate, to group important factors including, cancer stages and type of cancer, parity, and menopausal status that may affect lipid profiles in OC patients along with an investigation of new lipid profiles to clarify most lipid factors that may involve in OC development are needed.

Keywords: Ovarian cancer, lipid profiles, lipoproteins, serum lipids, lipids ratio.

1. Introduction

Ovarian cancer (OC) is the leading cause of death in all gynaecological malignancies [1]. The one-year survival rate for OC can be as high as 79% and when diagnosed in an early stage the 5-year survival rate is almost 95% [2]. The diagnosis of OC in the later stages was the primary cause of mortality in most cases. Early diagnosis is the key to reducing OC mortality rates. But even in late stages of the disease, the outcomes are highly variable. [3] Established risk factors for OC include family history and gene mutations, such as BRCA1 and BRCA2; while a decreased risk is associated with high parity, use of oral contraceptives, and breastfeeding, each of which suppress ovulation. Research has suggested that damage to the ovarian epithelium, resulting from repeated ovulation may play a role in the development of carcinoma at this site [2, 4–5].

Metabolic re-programming has recently emerged as a new hallmark of cancer. Alteration of cellular metabolism in cancer cells is proposed to increase the availability of essential building blocks that support uncontrolled cellular proliferation [6]. Cancer cells rely on *de novo* lipid synthesis for the generation of fatty acids to meet the needs of tumour growth, resulting in specific alterations in different aspects of lipid metabolism. These alterations can influence the availability of structural lipids for the synthesis of membranes, the production and degradation of lipids for energy supply and the abundance of lipids with signaling functions [7-8].

Lipids are the major macromolecules essential for various biological functions, including energy production, signaling, and cell growth and division. Defects in lipid metabolism are associated with several diseases, among which atherosclerosis, hypertension, obesity, diabetes, and cancer are the most important [9]. Among the factors that contribute to the appearance of cancer, diet has a fundamental role, and lipids are the main components that have been related to increases in the incidence of cancerous diseases, particularly breast, colorectal, ovarian, and prostate cancers [10].

The present study aimed to determine the alterations in serum lipid profile in OC patients in the north Indian population.

2. Materials and Methods

Total number of 300 subjects recruited from Out Patient Department (OPD) of Department of Obstetrics and Gynecology, King George's Medical University, Lucknow, Uttar Pradesh, India, after collecting information's regarding their age, medical, personal, family as well as a dietary history on a structured proforma. Study group comprised of 180 clinically and histopathologically approved cases of OC and control group comprised of age matched 180 apparently healthy individuals without any malignancies. However, information regarding case and control group subjects was collected by general questionnaire and history sheet after obtaining their informed consent. The study was approved by the institutional ethical committee and "we certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research".

Blood samples for measuring the serum lipid parameters were obtained in the morning after 12 h of fasting from an anticubotal vein under aseptic conditions. About 5 ml blood was collected from each subject into a plain vacutainer tube. The blood was allowed to clot and then was centrifuged at 3000 rpm for 15 minutes; serum was removed with the help of a pipette, and stored in -20°C for the analysis. The estimation of lipid profile was done within 6 hours of serum separation. Lipid profile concentrations (TG: triglyceride, TC: total cholesterol and HDL: high density lipoprotein) were determined using a commercially available kit (Merck kit) and a semi-automated analyzer (Microlab 300, Merck). Low density lipoprotein (LDL) and very low density lipoprotein (VLDL) were calculated by Friedewald equation [11]:

$$LDL= TC-(HDL+VLDL)$$
$$VLDL= TG/5$$

2.1 Statistical Methods

Data was analyzed using the statistical package program SPSS 16 version 3.0. Quantitative variables are presented as the mean ± standard deviation. Welch's corrected unpaired t-test was performed to assess the difference in biochemical parameters between the two groups. All Statistical tests were two-tailed, and $p < 0.05$ were chosen as the level of significance.

3. Results

In the present study, 180 healthy controls and 180 histologically confirmed cases of OC were included. In our study mean age of cases and controls were 44.10 ±12.39 and 42.33±11.45 years respectively. The distribution of age was almost equal among cases and controls. Significant differences were observed for most lipid parameters among study and control groups as shown in (Table 1). There was a significantly higher level of mean serum cholesterol (159.89±31.42 mg/dl), TGs (139.40 ±40.79 mg/dl), LDL-c (90.28 ±30.58 mg/dl) and VLDL (27.88 ±8.15mg/dl) found in OC patients as compared to the controls (cholesterol 155.30 ±23.82mg/dl, TGs (107.61 ±21.88 mg/dl), LDL-c (88.45± 25.31mg/dl) and VLDL (21.52±4.37 mg/dl). The HDL level is higher in controls (45.33 ±7.86 mg/dl) as compared to study group (41.72 ±4.85 mg/dl). TGs, HDL-c VLDL were found highly significant in OC patients compared to controls. The ratio of TC/HDL, LDL/HDL, HDL/LDL was also found significantly higher in OC patients as compared to controls (Table-1)

Table 1: Lipid profile values in study and control group

Parameters	study group (n= 180)	control group (n=180)	p value
Age (yrs)	44.10 ±12.39	42.33±11.45	0.160
TC	159.89 ±31.42	155.30 ±23.82	0.122
TG	139.40 ±40.79	107.61 ±21.88	<0.001*
HDL-c	41.72 ±4.85	45.33 ±7.86	<0.001*
LDL-c	90.28 ±30.58	88.45± 25.31	0.538
VLDL	27.88 ±8.15	21.52± 4.37	<0.001*
TC/HDL	3.87± 0.83	3.55 ±0.93	0.001*
LDL/HDL	2.33± 0.79	1.81 ±0.69	<0.001*
HDL/LDL	0.48± 0.18	0.65 ±0.35	<0.001*

Data are given as mean ± SD TC: total cholesterol; TG: triglyceride; HDL: high density lipoprotein; LDL: low density lipoprotein; VLDL: very density lipoprotein; *A value of $p < 0.05$ was considered statistically significant

On the basis of clinical stages of OC patients the lipid profiles levels were compared and calculated (Table-2 & Fig1). All four parameters (TC, TG, HDL-c, VLDL-c) shows an increase in serum levels with increase in the staging of the disease whereas the elevated serum level was not found statistically significant (p value not shown).

Table 2: Shows lipid profiles levels in clinical stages of ovarian cancer

Lipid Profile	Stage I (n=7)	Stage II (n=59)	Stage III (n=64)	Stage IV (n=50)
TC	157.69±29.58	158.99±31.07	160.41±30.94	162.10±31.21
HDL-c	41.88±4.87	43.69±4.88	45.71±3.89	48.72±4.88
TG	139.46±42.68	140.00±42.75	147.67±40.82	149.78±43.85
VLDL	27.89±7.53	28.93±8.16	30.56±6.15	33.95±8.17
LDL-c	87.92±29.49	89.35±30.20	90.71±30.32	105.42±30.38

Data presented in mean ± SD
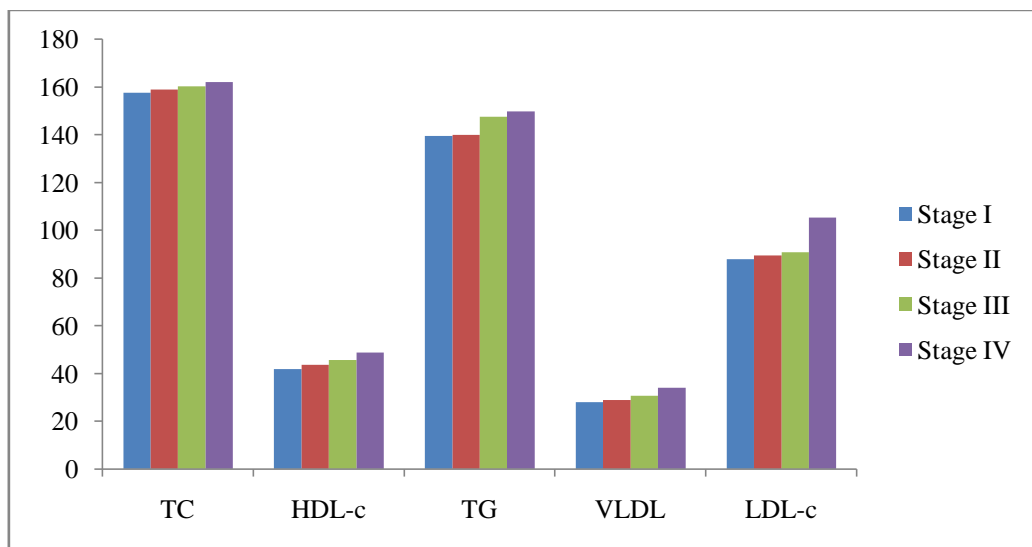
Figure 1: Shows comparison between mean serum values of lipid profile parameters in clinical stages of Ovarian Cancer

4. Discussion

Lipids have a primary role in the pathogenesis of coronary heart disease but researchers have reported an association of plasma/serum lipids and lipoproteins with various cancers. The question whether hypo or hyperlipidemia at analysis of malignancy is the causative component or after effect of disease has stayed unanswered [12]. Abnormal lipid metabolism, leading to increased lipid synthesis, is found to play an important role in the pathogenesis of malignancies [13]. The activity of lipid metabolizing enzymes is regulated by a complex interplay between metabolic and oncogenic signaling pathways [14]. In our study serum cholesterol level was found higher in OC patients as compared to healthy controls. Alterations in the circulatory serum cholesterol levels have been found to be associated with the etiology of breast cancer and colorectal cancer. However, only a few reports are available on plasma lipid profile in the head and neck cancer. [13]. In our study, we found significantly higher levels of TG, HDL-c, VLDL in OC patients as compared to control group. Our results are inconsistent with the study of Naik *et al*., 2006, which shows that serum TC, HDL-c and LDL-c significantly decreased and serum TG significantly elevated in leukemia and Hodgkin's disease patients. Many epidemiological studies have shown increased risk of death in cancer patients with low serum TC levels [15]. The elevation in lipid levels may be due to the reason that lipid maintains cell integrity and functionality of cell. The development of a malignancy requires the uncontrolled and excessive proliferation of cells. These newly formed cells need basic components well above the normal limits, used in physiological processes. One such component is lipid, which forms major cell membrane components essential for various biological functions including cell division and growth of normal and malignant tissues. The increased requirement of lipids to fulfill the needs of these new cells will diminish the lipid stores. This affects essential constituents of the cell membrane leading to greater utilization of lipids including, TC, lipoproteins and TG 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 [11-12, 16-18]. The increase in lipid levels was also reported in breast cancer [19], cervical cancer [12], head and neck cancer [11, 16] as well as oral cancer [21]. So our results have concordance with these studies. We reported that LDL level is slightly higher in OC patients than in healthy controls. This may be due to tumor cells expressing increased LDL receptor levels, which lead to low LDL levels [22]. In the present study the ratio of TC/HDL, LDL/HDL and HDL/LDL were also significantly higher in OC patients compared to healthy controls. Our study reports that lipid profile and advanced OC show a significant increase in TC, TG, HDL-C, LDL-C and VLDL was higher in the cases than in the control group. The likelihood that lipid abnormalities from the norm in cancer patients may speak to an intense stage reaction created by the conveyance of cytokines produced by inflammatory cells around the tumor or by the tumor cells itself. [23]. There are numerous studies indicating inverse relationship of lipid parameters with cancer. Variability of the estimations of plasma lipid profile in cancer patients may be because of numerous reasons, for example, age, nutritional status, body mass index, liquor utilization and activity propensities. The variability in the levels of parameters of lipid profile might likewise be because of methodological distinction [24]. It is accounted for that the evidently clashing studies are really predictable in light of the pattern of decrease in the serum cholesterol level slowly ten years going before the analysis of disease [16].

In conclusion, in the present study, we have estimated lipid profile in OC patients with healthy age matched controls. Our result shows that TC, TG, LDL-c, VLDL-c values higher in cases than in controls and the difference was significant, whereas HDL-c value is lower in cases as compared to controls and this difference is statistically significant. The ratio of lipid profile viz TC/HDL, LDL/HDL, HDL/LDL was found statistically significant and higher in cases in compression to controls. On compression among clinical stages of OC, all four parameters of lipid profile were statistically insignificant whereas level of all parameters increased from stage I to stage IV. This study shows that lipid parameters are not related with clinical stages of cancer. From this data we cannot conclude any confiding results. However, studies with more patients with long term follow up of cases and periodic estimation of lipid profile are needed, to establish the association between lipid profile and OC patients.

Conflicts of Interest

Acknowledgments

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