

Correlation of Lipid Profile with Cervical Cancer

Niharika N.*, Gomathy E.*, Shashidhar K.N.*

Abstract

Objectives: 1. Estimation of lipid profile parameters including triglycerides, total cholesterol, HDL cholesterol, LDL cholesterol and apolipoprotein A in both cases of carcinoma cervix and healthy controls. 2. Estimation of association of lipid parameters in cases with carcinoma cervix of various clinical stages. *Materials and Methods:* A total number of 60 women were recruited in our study. Out of these 60 women, 30 were cases and 30 were healthy controls. The 30 cases were clinically and histologically confined cases of carcinoma cervix of various stages. The 30 controls were matched with cases for age and BMI. The present comparative case control study was conducted at R. L. Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Academy of Higher Education, Tamaka, Kolar between January 2014 to June 2015. Lipid parameters were analyzed using Vitros 250 dry chemistry auto analyzer from Johnson and Johnson. Serum apolipoprotein A was analyzed by immunoturbidimetry. *Results:* The mean age for cases was 56.5 ± 12.03 and mean age for controls was 55.8 ± 10.16 . Majority of patients 14(46.7%) presented with three main symptoms i.e. offensive vaginal discharge, loss of appetite, weight loss. Majority of the cases, 18(60%) were postmenopausal women. Out of these 30 women who undergone biopsy, 28(96.7%) had squamous cell

carcinoma and 2 (3.3%) had adenocarcinoma. Amongst 30 cases, 9 patients (30%) had well differentiated, 19 had moderately differentiated and 2 had poorly differentiated carcinoma. Majority of patients 17(56.7%) presented with stage IIIB. The mean serum HDL, LDL, triglycerides, total cholesterol were 35.67 ± 8.16 , 79.47 ± 14.97 , 107.77 ± 28.11 , 131.7 ± 20.32 in cases respectively. The mean serum HDL, LDL, Triglycerides, total cholesterol were 50.47 ± 7.04 , 117.57 ± 22.89 , 183.57 ± 32.93 , 176.3 ± 24.24 in controls respectively. The mean serum apolipoprotein A levels in cases (169.19 ± 24.60) were increased when compared to controls. *Conclusion:* The mean serum HDL cholesterol, LDL cholesterol, triglycerides and total cholesterol were found to be significantly lower in patients with cervical cancer when compared to healthy controls. The mean serum Apolipoprotein A was found to be significantly elevated in cases when compared to healthy controls.

Keywords: Lipid Profile; Cancer Cervix; Apolipoprotein A.

Introduction

Cancer is defined as a relatively autonomous growth of tissue. It is a genetic disorder caused by DNA mutations that are acquired spontaneously or induced by environmental insults [1]. Cervical cancer is the third most common cancer in women worldwide accounting for 9% of all female cancer and 9% death in females due to cervical cancer. Worldwide it is seventh cancer with estimated 5,30,000 new cases in 2008 accounting for 4% of cancer worldwide. The world age adjusted rate is 15.2/100,000 population. More than 85% of the global

*Department of Obstetrics and Gynaecology, Sri Devaraj Urs Medical College, Kolar, Karnataka.

Niharika Nimmala, Post Graduate (Final Year), Department of Obstetrics and Gynaecology, Sri Devraj Urs Medical College, Kolar, Karnataka 563101.
E-mail: niharikanimmala888@gmail.com

burden is seen in developing countries and it accounts for 13% of all female cancer. In India, 1,34,000 women were detected to have cervical cancer, out of which 72,825 women died of cervical cancer in 2008 [2]. According to SurendraShastri, 1,82,027 new cases and 77,096 deaths occurred in India in 2010 due to cervical cancer [3].

Cervical cancer is a multi-factorial disease process and risk factors associated are early age of intercourse, multiple sex partners, low socioeconomic status and human papilloma virus infection [4]. Cancer development is a complex mechanism comprising of proliferation, apoptosis and differentiation and the interplay between these intricate processes decides tumor development and progression [5].

Lipids are major cell membrane components that are essential for various biological functions, such as maintaining cell integrity, cell growth and division of normal and malignant cells. Researchers have reported an association of plasma/serum lipids and lipoproteins with different cancers [6]. Reports suggest lipid peroxidation product malondialdehyde may cross link DNA on the same and opposite strands via adenosine and cytosine and may contribute to carcinogenicity and mutagenicity. Because of the lipid peroxidation there is a greater utilization of lipids probably total cholesterol, lipoproteins and triglycerides for the new membrane biogenesis in neoplastic state [8].

The purpose of the present study is to give an insight on the basics of lipids and also to evaluate alterations in plasma lipid profile in cervical cancer patients and its association with histological grading thus assisting in better understanding of these complex phenomena.

Aim and Objectives

1. Estimation of lipid profile parameters including triglycerides, total cholesterol, HDL cholesterol, LDL cholesterol and apolipoprotein A in both cases of carcinoma cervix and healthy controls.
2. Estimation of association of lipid parameters in cases with carcinoma cervix of various clinical stages.

Inclusion Criteria

Patients who were diagnosed to have cervical cancer of any clinical stage confirmed by biopsy were included as cases.

Exclusion Criteria

1. Obese individual with BMI >30.

2. Patients having other medical illness including diabetes, hypertension, hypothyroidism which interfere or alter lipid profile.
3. Patients who had previously taken or were at time of study on radiotherapy or chemotherapy.
4. Patients who were on medications such as statins, corticosteroid which are known to alter the lipid profile for past one month.
5. Patients who have undergone surgeries like bariatric surgery which are known to alter lipid levels.

Source of Data

The present comparative case control study was conducted at R. L. Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Academy of Higher Education, Tamaka, Kolar between January 2014 to June 2015. A total number of 60 women were recruited in our study after taking written and informed consent. Out of these 60 women, 30 were cases and 30 were healthy controls. The 30 cases were clinically and histologically confined cases of carcinoma cervix of various stages. The 30 controls were matched with cases for age and BMI.

Methodology

All patients were explained the details of the study and written, informed consent was taken from all cases and controls who were willing to participate in our study. All clinically suspected patients of carcinoma cervix underwent punch biopsy and endocervical sampling under aseptic precautions. The samples were sent to histopathological examination to confirm cervical cancer.

An overnight fasting blood sample of minimum 8 hours was collected from both cases and controls for estimation of serum lipid profile and apolipoprotein A. All possible standard precautions were used for sample collection. The blood was drawn from the left antecubital vein in sitting posture. Standard procedures were followed at every step to prevent hemolysis. 5ml of venous blood was drawn in plain vacutainer. It was centrifuged for 10 minutes at 3000rpm so as to separate out 2 ml of the serum. The serum was collected in aliquot tube and stored in the freezer at -80°C till analysis. Serum apolipoprotein A was analyzed by immunoturbidimetry. Lipid parameters were analyzed using Vitros 250 dry chemistry auto analyzer from Johnson and Johnson.

1. Total cholesterol.

2. Triglycerides. *Calculated Parameters*
3. HDL cholesterol. 1. LDL cholesterol by friedewald's formula.
LDL = TC-[(TG/5) + HDLc]
2. Apolipoprotein A.

Observations and Results

Table 1: Age distribution of patients studied

Age in years	Cases		Controls	
	Number	Percentage	Number	Percentage
31-40	4	13.3	4	13.3
41-50	5	16.7	5	16.7
51-60	13	43.3	13	43.3
61-70	5	16.7	5	16.7
71-80	3	10.0	3	10.0
Total	30	100.0	30	100.0
Mean ± SD	56.50±12.03		55.80±10.16	

Mean age for cases is 56.50±12.03.

Mean age for controls is 55.8±10.16.

Table 2: Distribution of symptoms in cases

Symptoms	Number of cases (n=30)	Percentage
Vaginal discharge	14	46.7
Post coital bleeding	7	23.3
Postmenopausal bleeding	11	36.7
Backache	14	46.7
Pain abdomen	11	36.7
Urinary symptoms	4	13.3
Loss of appetite	14	46.7

Majority of patients presented with the symptoms of offensive vaginal discharge, pain abdomen and loss of appetite.

Table 3: Menstrual status of cases and controls

Variables	Cases	Controls	P value
Age in years	56.50±12.03	55.80±10.16	0.809
Weight (kg)	52.14±6.74	53.53±8.15	0.473
Height (kg)	154.77±5.72	152.57±6.07	0.154
Waist circumference (cm)	81.50±5.76	84.43±8.44	0.121
Hip circumference (cm)	96.10±4.88	95.63±6.08	0.744

Majority of cases(60%) and controls(54%) were postmenopausal women

Table 4: Comparison of mean value of clinical variables in cases and controls

Lipoproteins	Cases	Controls	P value
HDL (mg/dl)	35.67±8.16	50.47±7.04	<0.001**
LDL (mg/dl)	79.47±14.97	117.57±22.89	<0.001**
Triglycerides (mg/dl)	107.77±28.11	183.57±32.93	<0.001**
Total Cholesterol (mg/dl)	131.70±20.32	176.3±24.24	<0.001**

Mean of all variables that is age, weight, height, waist circumference, hip circumference are matched with no statistical significance.

Table 5: Comparison of mean value of lipoproteins in cases and controls

Lipoproteins	Cases	Controls	P value
HDL (mg/dl)	35.67±8.16	50.47±7.04	<0.001**
LDL (mg/dl)	79.47±14.97	117.57±22.89	<0.001**
Triglycerides (mg/dl)	107.77±28.11	183.57±32.93	<0.001**
Total Cholesterol (mg/dl)	131.70±20.32	176.3±24.24	<0.001**

Table 6: Apolipoprotein A distribution in cases and controls

Apolipoprotein A (md/dl)	Cases		Controls	
	Number	%	Number	%
<150	7	23.3	27	90.0
150-200	19	63.3	3	10.0
>200	4	13.3	0	0.0
Total	30	100.0	30	100.0
Mean \pm SD	169.19 \pm 24.60		128.70 \pm 18.60	

The mean value for apolipoprotein A in cases was 169 \pm 24.60 and controls was 128.7 \pm 18.6.

Table 7: Histological type of carcinoma in cases

Type	No. of patients	%
Squamous cell carcinoma.	28	96.7
Adenocarcinoma.	2	3.3
Total	30	100.0

Majority of cases 28(96.7%) presented with squamous cell carcinoma

Table 8: Grades of carcinoma in cases

Grades	Number of patients	percentage
Well differentiated	9	30.0
Moderately differentiated	19	63.3
Poorly differentiated	2	6.7
Total	30	100.0

Majority of cases 19(63.3%) presented with moderately differentiated carcinoma.

Table 9: Stage of carcinoma in cases

Stage	Number of patients	Percentage
I	3	10.0
IIB	6	20.0
IIIA	3	10.0
IIIB	17	56.7
IV	1	3.3
Total	30	100.0

Majority of patients(56.7%) presented with stage IIIB

The mean serum HDL levels were lesser in cases (35.67 mg/dl) than in the controls (50.47mg/dl) which was statistically strongly significant ($p < 0.001$). The mean serum LDL levels were lesser in cases (79.47mg/dl) than in the controls (117.57 mg/dl) which was statistically strongly significant ($p < 0.001$). The mean serum triglycerides levels were lesser in cases (107.77mg/dl) than in the controls (183.57 md/dl) which was statistically strongly significant ($p < 0.001$). The mean serum total cholesterol levels were lesser in cases (131.7 mg/dl) than in the control (176.3 md/dl) which was statistically strongly significant ($p < 0.001$). There was statistically strong significant difference between the mean value of HDL, LDL, triglycerides and total cholesterol between the cases and controls.

Discussion

Cancer cervix is the most frequent cause of the death from cancer especially in women from

developing countries like India. Fundamentally the development of a malignancy requires the uncontrolled and excessive proliferation of cells. These newly forming cells would need many basic components well above the normal limits, used in physiological process. One such component is lipids which form 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 fulfil the needs of these new cells will diminish the lipid stores. As many studies were not done comparing lipid profile with carcinoma cervix, we are comparing the present study results with lipid profile of other malignancies.

In our study, majority of cases 13 (43.3%) belonged to age group 51-60 years. The mean age for cervical cancer was 56.5 years in present study. In studies done by Saraswathmali et al, Bhadury et al majority of their cases belonged to age group 31-50 years. In 2010 Naryana SM et al conducted a study on scenario of cervical in Kolar at our hospital which showed

majority of cases 46(42.59%) were in age group 41-50 years which was not correlating with present study. On histological examination squamous cell carcinoma was the commonest type and it was correlating with studies done by Narayan SM et al.

Majority of cases 20(66.7%) in present study belonged to stage III of cervical cancer. Similar results were seen in study done by Narayana SM et al at Kolar in 2010 in our hospital, which showed maximum number of patients 83(76.83%) presented with stage III of cervical cancer. In present study most of the patients had come with locally advanced stage of cancer compared to other studies. As Kolar is a rural area cultural attitude and lack of public education also discourage early diagnosis. Most of the patients presented to our hospital with advanced stage of cancer

It was seen that the mean serum total cholesterol levels were lesser in carcinoma group (131.7 mg/dl) than in the control group (176.3 md/dl) which was statistically strongly significant ($p < 0.001$). Similar results were seen in studies done by Naik P.P et al ($p < 0.001$), Patel P.S et al ($p < 0.008$), Raju K et al ($p < 0.079$). The serum total cholesterol were elevated in study done by Ali et al ($p < 0.039$). In breast cancer the total cholesterol is elevated compared to controls. Zhang Xi et al reported that adult weight gain or increased BMI is a strong predictor of breast cancer risk [6]. Cholesterol is essential for maintenance of the structural and functional integrity of all biological membranes. Cholesterol is an essential constituent of lipoprotein fraction. Low serum levels of cholesterol could be due to the ongoing process of oncogenesis

It was seen that the mean serum triglycerides levels were lesser in carcinoma group (107.77mg/dl) than in the control group (183.57 md/dl) which was statistically strongly significant ($p < 0.001$). Similar results were seen in studies done by Patel P.S et al ($p < 0.059$), Raju K et al ($p < 0.02$), Neerupakam M et al ($p < 0.001$). The triglycerides values were elevated in studies by Ali et al ($p < 0.043$), Naik. P.P et al ($p < 0.001$) which was not correlating with present study. The possibilities for decrease triglycerides may be due to decreased synthesis or increased catabolism or synthesis of lipoproteins and cholesterol by the liver could be inhibited by tumour metabolites.

It was seen that the mean serum HDL levels were lesser in carcinoma group (35.67 mg/dl) than in the control group (50.47mg/dl) which was statistically strongly significant ($p < 0.001$). Similar results were seen in studies done by Naik P.P et al ($p < 0.001$), Neerupakam M et al (0.043), Patel P.S et al ($p < 0.001$). No statistical difference in mean serum HDL levels were seen in study by done Raju K et al ($p < 0.355$), Ali

et al ($p < 0.32$). As tumour cells accumulate cholesterol as CE in lipid droplets and efflux less cholesterol to HDL, thus results in decreased HDL cholesterol.

It was seen that the mean serum LDL levels were lesser in carcinoma group (79.47mg/dl) than in the control group (117.57 mg/dl) which was statistically strongly significant ($p < 0.001$). Similar results were seen in studies done by Naik.P.P et al ($p < 0.001$), Neerupakam M et al ($p < 0.004$), Patel P.S ($p < 0.04$). No statistical difference in mean serum LDL levels were seen in study done by Raju K et al ($p < 0.119$), Ali et al ($p < 0.18$). The decreased may be due to elevated expression of LDL-R in malignant cells increases the uptake of LDL via receptor mediated endocytosis. High consumption of LDL by cancer cells may cause depletion of LDL from serum of cancer patients.

Feng Sua and colleagues studied Apolipoprotein A-I (apoA-I) and apoA-I mimetic peptides inhibit tumor development in a mouse model of ovarian cancer and concluded mice expressing a human apoA-I transgene had increased survival ($P < 0.0001$) and decreased tumour development ($P < 0.01$), when compared with littermates, following injection of mouse ovarian epithelial papillary serous adenocarcinoma cells (ID-8 cells) [7]. ApoA-I mimetic peptides reduced viability and proliferation of ID8 cells and cis-platinum-resistant human ovarian cancer cells, and decreased ID-8 cell-mediated tumour burden.

Research has shown that exogenous ApoA1 prevents tumour development in mice, while lowered APoA1 levels are associated with ovarian cancer. ApoA1 has been shown to have anti-inflammatory and antioxidant capabilities in addition to counteracting atherogenesis. No studies are done regarding the association of apolipoprotein A and carcinoma cervix. In present study, it was seen that the mean serum Apoprotein A levels were greater in carcinoma group (169.19 mg/dl) than in the control group (128.7mg/dl) which was statistically strongly significant ($p < 0.001$).

Conclusion

Our study concluded that the lipid parameters and apolipoprotein A were significantly different in cases and controls. The mean serum HDL cholesterol, LDL cholesterol, triglycerides and total cholesterol were found to be significantly lower in patients with cervical cancer when compared to healthy controls. The mean serum Apolipoprotein A was found to be significantly elevated in cases when compared to healthy controls. Periodic estimation of lipid profile

in patients with suspected cases of cervical neoplasia will help us to establish the association between lipid parameters and cervical cancer. Thus the lipid profile can be used as a diagnostic or prognostic marker for cervical cancer.

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