SERUM CHOLESTEROL LEVELS AND INCIDENCE OF OVARION TUMOURS IN PAKISTANI WOMEN

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Background: This study was aimed to observe the relationship of serum cholesterol with incidence of ovarian tumours (benign and malignant) in pre and postmenopausal Pakistani women. Effect of type (benign and malignant) and state of disease (FIGO stages of malignant tumours) on serum was also the objective of the study. **Methods**: Thirty-five clinically and histopathologically confirmed patients with benign & malignant tumours (mean age 47.05 with rang of 16–70 years) selected. Nineteen age and weight matched healthy control subjects were selected among the female staff members and students of JPMC. Serum cholesterol was estimated by kit method. **Results**: In case of benign tumour patients lowest level of serum cholesterol was observed in serous cyst adenoma ($p<0.0005$) & ovarian cyst of undetermined origin ($p<0.001$). The lower cholesterol levels were also observed in other groups when compared with controls ($p<0.0005$). Statistically significant differences were noted when serum cholesterol levels compared between stage 1 and III ($p<0.05$) between 1 and 1V ($p<0.001$) II & 1V ($p<0.05$) and between III & 1V ($p<0.01$). **Conclusion**: Findings of this study suggests that lowest levels of total cholesterol (TC) has been observed in various s benign and malignant tumours and the inverse correlation between low total cholesterol levels to incidence and mortality of tumours is more markedly associated with the advance disease status. This finding of inverse relation of TC with increase incidence of cancer is in agreement with the several prospective epidemiological studies carried out by various researchers.

Key words, Serum Cholesterol, Ovarian tumours, Incidence in Pakistan

INTRODUCTION

Among females, ovarian cancer accounts for almost 90% of malignancies in Western world[1]. Incidence of cancer is steadily increasing in developing countries. At present the distribution of cancers between the developing and developed countries is similar[2-3]. Ovarian cancer amongst the commonest killer of female pelvic malignancies and has by far the worst prognosis among the gynaecological cancers[4]. As a group cancer comprise the most common contribution in non-cardiovascular mortality and examination of cancer including ovarian cancer incidence by cholesterol level might be accepted to show higher incidence at lower levels. Cholesterol is almost found exclusively in animals and humans, virtually all cells contain some cholesterol. There is wide evidence that cholesterol is essential to and intimately involved with many aspects of cellular structure and function for example it affect the fluidity of cell membranes, membrane permeability, signal transmission and other cell properties. It is the precursor for synthesis of vitamin D, steroid hormones and bile acids[5]. Several prospective epidemiological studies set up mainly to examine the association of baseline blood concentration of cholesterol with subsequent rate of coronary heart disease, have also examined its association with subsequent rates of cancer[6-12]. All of these studies have found an inverse relationship between cholesterol concentration and the subsequent risk of various types of cancers. This stud was aimed to observe the relationship of serum cholesterol levels with incidence of ovarian tumours (benign and malignant) in pre and postmenopausal Pakistani women. Effect of type (benign and malignant) and state of disease (FIGO stages of malignant tumours) on serum cholesterol was also the objective of this study.

MATERIAL AND METHODS

Clinically confirmed 35 patients with benign & malignant tumours were selected from departments of gynaecology and obstetrics, of Jinnah Postgraduate Medical Centre (JPMC), Civil Hospital, Abbasi Shaheed Hospital, Lady Differen Hospital and Sobraj Maternity Home Karachi. All the patients were provisionally diagnosed as ovarian tumours and diagnosis was confirmed by reviewing operation notes and histopathological reports. Their personal and family history was taken. They were also physically examined and positive findings were noted. These patients were further classified into two groups *viz* benign and malignant. These malignant ovarian tumours were classified according to FIGO (International Federation of Obstetrics and Gynaecology) staging. The tumours were further classified histologically as serous, mucinous, mixed serous endometriod, endometroid alone and granulose cell tumours. In benign ovarian tumour patients the tumours were categorized as serous cyst adenoma.

Endometriosis, cyst of undetermined origin, follicular and paraovarian cyst. Nineteen age and weight matched control subjects were selected among the female staff members and students of JPMC, Karachi, who did not have history of malignant or other chronic diseases, and any medication (hormone or other). Mean age of the study subjects was 47.05 years with rang of 16–70 years.

Fasting venous blood samples were taken with disposable syringe. The blood samples were allowed to clot in the syringe at the room temperature for about 30 minutes. To obtain serum the clotted blood samples were centrifuged at 3000 rpm for at least 10 minutes. The cleared serum was then transferred (5 ml) glass tubes for storage in the freezer at -20 °C until assayed. Serum cholesterol was estimated by enzymatic colorimetric method using kit Cat No. Cod: 1001091 supplied by Reactivos Spinneret, Spain.

RESULTS

This study included thirty-five patients of ovarian tumours. On histopathological examination. Nineteen of these patients were diagnosed as malignant tumours while remaining 16 turned out as benign tumours (Table-1). In the malignant group according to FIGO staging there were 8 patients in stage I, 4 patients in stage II, 3 patients in stage III and 4 patients in stage IV.

The histological finding of malignant tumours suggested these histological classes, serous (2.8%) mucinous (15.8%), mixed serous endometroid (10.5%) endometroid alone (10.5%) and granulose cell tumours (10.5%). In benign tumour category the histological findings revealed these types: serous cyst adenoma (43.75%) comprising the largest proportion, endometriosis (18.7%), cyst of undetermined origin (12.5%) and follicular and paraovarian cysts (25%).

Table-1: Serum cholesterol levels in control subjects and benign and malignant ovarian tumour patients

	Control	Ovarian tumours	
		Benign	Malignant
Number of subjects	19	16	19
Cholesterol (mg/dl)	189.73 ±6.56	133.16 ±7.30	124.06 ±11.61

In case of benign tumour patients lowest levels of serum cholesterol were obtained in serous adenoma and ovarian cyst of undetermined origin. The low serum cholesterol levels were also observed in other groups when compared with control values as shown in Table-2.

When serum cholesterol levels were compared among various stages of malignant ovarian tumours, there was no statistical significant difference between the cholesterol levels observed in stage I and II and between II and III, but statistically significant differences were noted when values were compared between stage I and III ($p<0.05$), between I and IV ($p<0.001$), between III and IV ($p<0.01$), indicating that inverse correlation of cholesterol level is more marked in advanced stages of disease as shown in Table-3 and 4.

Table-2: Serum levels of cholesterol (mg/dl) in control and various groups of benign ovarian tumours

Parameters	Controls (n=19)	Group A (n=7)	Group B (n=2)	Group C (n=3)	Group D (n=4)
Cholesterol (mg/dl)	189.73±6.56	120,428±9.66 *p*<0.005	120.0±1.4 *p*<0.01	162.0±26.71 *p*<0.05	140.25±9.3 P<001

P values are vs. control values. Group A: Serous cyst adenoma and adenomata. Group B: Ovarian cyst of undetermined origin. Group C: Endometriosis. Group D: Follicular + paraovarian cysts.

Table-3: Serum levels of cholesterol in controls and various groups of malignant ovarian tumours.

Parameters	Controls (n=19)	Group A (n=10)	Group B (n=3)	Group C (n=2)	Group D (n=2)	Group E (n=2)
Cholesterol (mg/dl)	189.73±6.56	98.44±9.11 *p*<0.0005	147±48.76 *p*<0.0005	149±7.7 *p*<0.0005	174±6.3 *p*<0.005	142.75±5.12 *p*<0.005

P values of various groups given in the table-3 are vs. control values. Group A: Serous cyst adenocarcinoma. Group B: Mucinous cyst adenocarcinoma. Group C: Mixed serous endometrioid carcinoma. Group D: Endometrioid carcinoma. Group E: Granulosa cell tumour.

Table-4: Serum cholesterol levels in various stages of malignant tumours (FIGO staging)

	Stage-I	Stage-II	Stage-III	Stage-IV
Number of Patients	8	4	3	4
Cholesterol (mg/dl)	143.3±18.6	159±63.56	107±9.23	63.2±14.86

DISCUSSION

Rose *et al* first reported an association between lower cholesterol concentrations and increase risk of cancer in 1974 for cancer of colon[13]. Such an inverse relation has since been found in several other major prospective studies for all cancers together[2,6-8,10,11,14,16] and for three specific cancers (lung, colon, and leukaemia)[2,10,13,17,18]. The raised mortality rate related to low cholesterol values in elderly people is

commonly attributed to cancer, as in younger people. From Australian age and cause specific mortality rates Dugdale estimated that lowering the serum cholesterol of the whole population by 10% should lengthen median life by 1 year, but the percentage of deaths from cancer should rise from 26.8 to 29.6%[6].

Since long serum total cholesterol level has been inversely related to the incidence of various cancers. Jacobs *et al* reported that total cancer death rate for those women having total cholesterol (TC) level less than 160 ml/dl was greater than for those having TC level 160–199 mg/dl in 6 of eleven studies[10]. Williams *et al* detected a positive correlation between low serum cholesterol and incidence of common cancers in women[19]. In the present study, TC levels observed in malignant group was significantly low, when compared with the controls with $p<0.0005$ (having mean value 124.6±11.61 and 189±6.59 mg/dl respectively). On the other hand, there is no specific difference, when TC level of benign patients were compared with those of control subjects. This inverse correlation between TC levels and incidence of tumour is more markedly associated with the advance disease status, as in this study. Three patients (stage IV), were having minimum TC level in all groups. This finding of present investigation is in accordance with that reported by Schatzkin *et al*[20]. It is hypothesized that serum cholesterol reflects cholesterol synthesis, as in one experiment Wynder *et al* found that the ability of lymphocytes to detect and kill tumour cells was substantially diminished in lymphocytes with impaired ability to reduce cholesterol[21]. Vitol *et al* demonstrated an inverse correlation between disease activity and plasma cholesterol in cases of acute leukemia[18] and Avail *et al* confirmed that the same mechanism is applicable with patients suffering from ovarian cancer[22].

CONCLUSION

Since long serum total cholesterol has been inversely related to incidence of various cancers and a number of studies has reported that total cancer death rate for those women having low total cholesterol are greater and various possible mechanisms have been postulated in causation of cancer and cancer deaths related to total cholesterol. Further systematic investigation is recommended of possible links between cholesterol metabolism and specific cancers or other disease processes that may be associated with low cholesterol.

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