CHOLESTEROL AND LIPIDS IN CANCER PATIENTS

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SUMMARY

Fifty biopsy proven cancer cases were studied after excluding liver and kidney disorders for changes in lipids metabolism with special reference to fasting serum Triglycerides (TG), Total lipids, Cholesterol, High Density Lipoprotein-Cholesterol (HDLc), and Low Density Lipoprotein-Cholesterol (LDLc). Significant changes were observed. Comparing different groups of cancer patients Vs controls, TG level was 157+19.03 and 204.86+23.41 mg/dl ($P<0.05$), cholesterol was 172.92+6.54 and 213.86+9.87 mg/dl ($P<0.01$) HDLc was 32.17+1.41 and 38.2+1.65, LDLc was 113.6+55.62 and 134.7+7.85 mg/dl ($P<0.05$) respectively. TG and Cholesterol levels were below the normal control levels in 78% and 54% of the cases respectively. In 56% of cases total lipid level was within the normal control level while in 28% of the cases it was below the normal range. HDLc and LDLc levels were below the normal control level in 62% and 70% of the cases respectively. Low levels of cholesterol and TG were estimated in patients with malignancies of different organs. However cause and effect relationship could not be established.

INTRODUCTION

Cholesterol is widely distributed in body cells and is an important constituent of plasma membrane and plasma lipoprotein, particularly the nervous tissue. It is the parent compound of all the steroids synthesized in body. Though cholesterol excess is linked with coronary diseases, its deficiency is debated as a cause of death in other diseases especially cancer. Pretreatment plasma cholesterol levels are significantly lower in patients with cancer. Triglyceride levels also appear to have potential as indicator of risk of death in patients with prostate cancer.[1] Cancer patients usually die when their serum proteins, albumin and cholesterol are lower than half the initial level.[2-5]

Incident cancer cases have significantly lower mean serum cholesterol levels at intake than the non-cancer population. The association between cholesterol and cancer tends to be stronger overall for males than females.[6] Serum cholesterol level is inversely associated with incidence of colon cancer and with other sites only in men; these inverse associations are statistically significant after adjustment for age, alcohol consumption, cigarette smoking, education, systolic blood pressure and relative weight.[7]

Most of the studies undertaken to evaluate the role of lipids as a tumour marker are either specific for a group or single cancer site or lacked the exclusion criteria. This study covers a wide range of cancer types and sites, excluding other liver and kidney disorders, which may affect lipid levels in a cancer patient.

MATERIAL AND METHODS

Present study was aimed to elucidate facts about altered cholesterol metabolism

in cancer cases and explain the current hypothesis concerning low cholesterol concentrations. Fasting total cholesterol, HDL-cholesterol, triglycerides and total lipids were proposed to be carried out in all eligible cancer and control patients.

Only those patients and controls were eligible for study whose following tests were normal. Fasting blood glucose, aspartate amino transferase (AST), alanine aminotransferase (ALT), gamma glutamyl transpeptidase, alkaline phosphatase, prothrombin time, total bilirubin, total protein, creatinine, albumin and A/G ratio.

Pretreatment patients of different types of malignancies were selected from those admitted in surgical, medical or cancer wards, or those attending as outdoor patients of Radiotherapy Department, Jinnah Postgraduate Medical Centre, Karachi.

Patients were classified into the following groups:

	Groups	No. of cases
1.	Epithelial tumours	38
	a. Carcinoma	10
	b. Adenocarcinoma	28
2.	Non epithelial tumours	12
	a. Sarcoma	5
	b. Leukemia	6
	c. Astrocytoma	1
	Total	50

Apparently 15 normal healthy individuals of the same age, sex and socio-economic status with no family history of cancer were selected as control subjects. They were selected from the staff and students of the Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, Karachi. Clinical history of the patients such as age, weight, blood pressure, family history, duration of the disease were also recorded.

Sample collection :

About 10 ml of blood was drawn from the cubital vein of patients and controls after an overnight fast for 12-14 hours. The blood was transferred into dry culture tube and allowed to clot at 37°C in a water bath. Serum was separated, 05 ml serum was taken in a plastic cap tube for glucose and liver function tests estimation immediately. Remaining serum was stored in plastic capped bottles in deep freezer at -20°C for further tests. All samples were analysed simultaneously to avoid effects of alternate freezing and thawing.

RESULTS

Mean age of the control group was 49.4 years and that of the patients was 48.73 years. No significant difference was observed between average age of normal control and cases. (Table–I) Serum AST was significantly raised in individual groups of studied cases but the level was within normal limits in total number of patients. Serum ALT was not significantly changed in cases as compared to controls. Similarly GGT levels in serum was also with in the normal limits in controls as well as in cases, no significant change was observed. ALP levels in serum of patients with epithelial carcinoma was significantly raised ($P < 0.05$) as compared to controls. It was also high in patients with adenocarcinoma. Non epithelial tumours showed no significant change, however, the levels were increased.

Serum TG (Table–II) levels was significantly decreased in carcinoma and non-epithelial group, whereas in adenocarcinoma group the decrease was markedly significant ($P < 0.01$), Serum cholesterol levels were significantly decreased in both the epithelial groups ($P < 0.05$). In total number of cases it also showed marked difference ($P < 0.01$). In carcinoma groups the decrease in total lipids was markedly significant ($P < 0.01$). Whereas in adenocarcinoma and non-epithelial tumours the decrease was

TABLE – I

Groups	Age (years)	AST (U/l)	ALT (U/l)	GGT (U/l)	ALP (U/l)
Controls (15)	49.4±2.56	22.4±2.01	34.79±7.25	34.97±7.34	91.93±7.52
Epithelial Tumours					
i. Carcinoma (23)	52.71±2.09	28.71±1.95	23.27±2.46	34.03±5.36	120.57±9.52
ii. Adeno Carcinoma (10)	44.4±3.01	44.4±3.01	20.96±5.84	37.07±13.22	135.50±39.25
iii. Total (38)	50.52±1.81	29.89±2.16	22.92±2.29	34.83±5.16	124.44±12.18
Non-Epith Tumours (12)	43.08±6.19	43.08±6.19	23.75±5.05	36.31±6.57	130.75±82.00
Total cases (50)	48.73±2.04	25.74±2.50	23.12±2.09	35.19±4.28	124.00±10.64

highly significant ($P < 0.001$). Serum HDL-cholesterol decreased slightly in carcinoma groups whereas in adenocarcinoma and non-epithelial tumours the decrease was markedly significant ($P < 0.01$) and highly significant ($P < 0.001$) respectively as compared to normal controls. Serum LDL-cholesterol showed slight decrease in epithelial tumours, whereas in non-epithelial group the decrease was significant ($P < 0.001$). In adenocarcinoma and non-epithelial group the decrease in total lipids was markedly ($P < 0.01$) and highly significant ($P < 0.001$).

Serum triglycerides were significantly reduced in cases of lung, bladder, larynx and maxilla (Table–III). Total lipids level was significant in the cases of tongue, cheek and maxilla. However, the difference in cases of bladder, colon and leukaemia were markedly significant. Breast cases showed high difference ($P < 0.001$). Serum cholesterol levels decreased markedly in cases of bladder, colon and leukaemia ($P < 0.01$). HDL-cholesterol was significantly reduced in cases of leukaemia ($P < 0.05$). Whereas in case of colon the difference was markedly significant ($P < 0.01$). Serum LDL- choles-

TABLE – II

Groups	T-LIP (mg/dl)	HDLc (mg/dl)	LDLc (mg/dl)	TG (mg/dl)	CHOL (mg/dl)
Controls (15)	935.66±49.45	38.20±1.65	134.70±7.85	204.86±23.41	213.86±9.87
Epithelial Tumours					
i. Carcinoma (28)	707.85±49.14	36.46±1.67	119.63±6.03	149.10±12.78	185.89±7.17
ii. Adeno Carcinoma (10)	579.60±50.90	27.31±2.78	114.27±16.22	122.00±10.17	162.4±17.49
iii. Total (38)	674.07±39.38	34.05±1.56	118.22±6.05	142.00±10.17	179.71±7.08
Non-Epith Tumours (12)	580.41±52.02	26.2±2.58	98.96±13.02	111.07±17.5	151.41±14.34
Total cases (50)	651.6±32.69	32.17±1.41	113.60±5.62	157.4±19.03	172.92±6.54

terol level was decreased significantly ($P < 0.05$) in case of bladder and markedly in case of leukaemia ($P < 0.01$), whereas change in case of colon was highly significant ($P < 0.001$).

DISCUSSION

Cholesterol is an important constituent of atherosclerotic plaque. In highly developed nations where coronary heart disease is the leading cause of death, much attention has been focussed on the serum cholesterol-coronary heart disease relationship, while little attention has been paid to the relationship between the level of serum cholesterol and other diseases such as cancer.

Rose and Shipley found a J-shaped relation between total mortality and cholesterol concentrations measured at the entry of the study. This shape resulted from a strong positive relation of plasma cholesterol with deaths from coronary heart disease (CHD) combined with an opposite (inverse) relation between plasma cholesterol and deaths from other causes. Cancer mortality was 66% higher in the group with the lowest plasma cholesterol than in the group with the highest plasma cholesterol. Statistically significant inverse relation of serum cholesterol to mortality from cancer of colon, lung and malignancies of haemopoetic and lymphatic system were quoted.[8,9]

In Yugoslavia cardiovascular disease study, the negative association of serum cholesterol and subsequent mortality appeared to be due to deaths from cancer and respiratory diseases.[8] The inverse relation of baseline serum cholesterol to subsequent 9 years mortality in a cohort of Japanese American men, was statistically significant only for colon cancer and lung cancer among the common sites as well as for malignancies of the lymphatic and hematopoietic system.[9] Similar findings were reported in a five years study in 10,000 middle aged in Malo, Sweden.[10]

In Puerto-Rico Heart Health program, serum cholesterol measured at first examination was found to vary inversely with

TABLE – III

Groups	TG (mg/dl)	LIP (mg/dl)	CHOL (mg/dl)	HDLc (mg/dl)	LDLc (mg/dl)
Controls (15)	204.86±23.41	935.66±49.44	213.86±9.87	38.2±1.65	134.70±7.85
Epithelial Tumours					
Lung (6)	123.83±16.9	757.5±106.5	195.5±12.97	37.51±2.48	133.21±8.23
Bladder (5)	108.6±23.56	540±114.22	145±21.05	35.62±4.52	87.60±19.59
Larynx (4)	133.75±15.76	660±171.41	189.75±12.45	35.57±6.23	127.42±12.01
Oesophagus (4)	182±26.11	790±84.92	209±15.56	35±4.29	137.57±12.06
Tongue & Cheek (6)	163.5±29.39	660.33±102.49	186.66±16.01	36.2±4.78	117.9±9.48
Breast (4)	160.5±15.31	668.75±48.74	204.25±24.82	34.45±2.60	146.7±30.42
Colon (2)	107±33	450±130	112±24	21.25±4.65	69.35±12.75
Non Epithelial Tumours					
Maxilla (3)	121.33±15.60	658.3±102.88	175.33±22.18	34.66±2.42	116.4±19.47
Leukaemia (4)	162.25±36.83	568.75±82.62	132±20.78	25.65±4.86	73.9±15.90

subsequent mortality from cancer with a greater percentage being oral, pharyngeal and stomach and a lesser frequency being lung.[11] In present study we have observed low serum cholesterol values in cancers of bladder, colon and leukaemia, which were markedly significant. Lower values of cholesterol in leukaemic cells might be due to a more rapid rate of utilization of cholesterol for cellular growth or to a more rapid efflux of cellular cholesterol, eliciting a higher LDL receptor activity.[12] Gilbert and Ginsberg found the same results in chronic myelocytic leukaemia.[13]

In Honolulu Heart Programme, there were trends of inverse association of all non cardiovascular diseases with total cholesterol and low density lipoprotein cholesterol.[14] Cancer patients as a group demonstrated significantly lower total cholesterol, esterified cholesterol and HDL-cholesterol, compared with non cancer patients. Breast cancer proved to be an exception associated with increased serum total cholesterol, free cholesterol, LDL-cholesterol and triglycerides.[15]

In acute myelogenous leukemia cells, cholesterol turnover was found to be more rapid than in normal mononuclear cells. The resultant depletion of cholesterol elicits both a higher LDL receptor activity and a higher rate of cholesterol synthesis in these leukemic cells.[12] The rate of receptor-mediated degradation of ^{125}I-LDL in cells from patients with acute myelogenous leukemia was markedly higher. Leukemic cells from patients with monocytic (FAB-M5) or myelomonocytic leukemia (FAB-M4) exhibited the highest degradation rates. It was also high in leukemic cells from patients with chronic myelogenous leukemia in blast crisis and in patients with acute undifferentiated leukemia. In contrast, leukemic cells from patients with acute lymphoblastic leukemia showed low rates. Hypocholesterolemia was a frequent finding in the leukemic patients. There was an inverse correlation between the plasma cholesterol level and rate of receptor-mediated ^{125} I-LDL degradation by leukemic cells.[16] LDL-receptor activity was found to be inversely correlated with plasma cholesterol concentration in acute leukemia. Hypocholesterolemia in leukemia and other neoplastic disorders may be due to increased LDL-receptor activity in malignant cells.[17] Tumour load, the presence of an enlarged spleen and changes in lipid metabolism of circulating cells in a patient with chronic myelocytic leukemia, all appear to contribute to the reduction in LDL cholesterol levels.[13] Gilbert et al. found significantly lower total and LDL cholesterol levels in men with myeloproliferative disease.[18]

The findings of the present study are also in agreement with the above studies.[2,4-6,15,19] Sidney and Farquhar found inverse relationship between cholesterol and cancer which was most consistent for large bowel in male patients only.[20] Our results are also in accordance with Williams et al. who observed inverse association of serum cholesterol with colon cancer and cancers of other sites only in men. Mean serum HDL-cholesterol in controls verses cases was 38.2 $\pm$ 1.65 mg/dl and 32.17 $\pm$ 1.41, and LDL-cholesterol was 134.70 $\pm$ 7.85 and 113.60 $\pm$ 5.62 respectively. These findings are in accordance with Alexopoules et al. who observed a decrease in total cholesterol and HDL-cholesterol in all cancer types except breast cancer. Total lipids decreased significantly in cases of carcinoma bladder, tongue and cheek, breast colon, Maxilla and leukaemia. Whereas serum triglycerides decreased significantly in carcinoma of lung, bladder, larynx, colon and maxilla.

Further studies are needed to evaluate these abnormalities, to establish a cause and effect relation and to exercise precautionary measures to protect the patients from cancer.

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