



Estimation of Serum Lipids in Colorectal Carcinoma: A Prospective Study

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Abstract

To investigate the correlation between lipid metabolism disorder and the occurrence and development of colorectal cancer by monitoring the alteration in lipid levels in cancerous tissue and serum in patient with colo rectal cancer. Abnormal lipid metabolism has been found to be associated with several type of cancer, whether this association is due to altered lipid metabolism taking place after tumor formation or due to altered metabolism favorable for tumor formation is not clear.

Keywords: Colo rectal carcinoma, lipid profile.

Introduction

Colorectal carcinoma is the third most common cancer in men (10% of total cancers) and the second in women (9.4% of total cases) worldwide with approximately 18,000 patients dying every year in U.K. In India Hospital based and Population based data also show that the incidence rate of rectal cancer is higher than colonic carcinoma in all parts of India. Most of the cases of Colorectal Carcinoma commonly present late in its progression. It is a disease in elderly with 90% cases presenting beyond 50 years of age.

This cancer has different forms such as familial, hereditary and sporadic. It is now accepted that Colorectal Carcinoma arises from adenoma in a stepwise progression in which increasing dysplasia in adenoma is due to an accumulation of genetic abnormalities (the adenoma-carcinoma sequence). Usually, this carcinoma presents as an ulcer, but polypoid & infiltrating types are also

not uncommon. There is also increased incidence of this disease in patients with some other disease or abnormal states like adenomas, villous papilloma of large bowel, ulcerative colitis and Crohn's disease.

The most popular hypothesis explaining the development of adenoma-carcinoma in colon and rectum are based on environmental factors and particularly with the variations in dietary habit. According to Burkitts hypothesis the diet and fecal constituents are important in etiology of cancer in large bowel, which attribute to low-residue diet high in refined carbohydrate & low in fiber. A more recent study of British vegetarians, found a 12% non significant increase in Colorectal Carcinoma among these vegetarians in comparison to meat eaters. The multi European studies show a small inverse association between intake of total fruit and vegetables and Colorectal Cancer risk in non tobacco users.

Among various other factors associated for etiological risk factor of this dreaded malignancy in different literatures, some consider serum lipid profile is one of the etiological risk factors among them. Some studies state that it is positively correlated with Colorectal Carcinoma & some studies state that it is negatively correlated. Lipid is the key components of the cell membrane, dyslipidemia has been associated with an increase risk factor for CRC(1,2) whether increases 12,13,3,4,5,6 or decreases 7,8,9,10 or has no effect 11on mortality rate is still controversial. In recent years, a large no of studies have demonstrated that abnormal levels of lipids closely co related with the initiations and progression of breast cancer 14,15. In particular, there have been a no of reports in the literature regarding the relationship between abnormal lipid levels and colo rectal carcinoma, 16-19

Hence, keeping the above facts in causation of colorectal carcinoma, this present study may throw some light in linking the disease with the levels of serum lipids, so that in future it may help in reducing the incidence by taking appropriate dietary and other measures.

Materials and Methods

The present piece of work embodied in the thesis “Estimation of serum lipids in colorectal carcinoma: a prospective study”, was undertaken in the department of General Surgery, VIMSAR, Burla from November 2014 to November 2016. The mode of selection of cases and the procedures followed in this study are detailed below.

Selection of cases

Cases were selected randomly among the admitted patients in the department of General Surgery, both in emergency as well as through the outpatient departments and also in the Radiotherapy department. The cases were diagnosed to be suffering from carcinoma of the colon and rectum, both by through clinical examinations as well as through proper investigations. 40 cases of carcinoma of different parts of the colon and rectum on different stages

and of different age groups were selected randomly. Both male and female patients were taken in the study after the diagnosis is confirmed. 40 cases of patients suffering from other diseases but not colorectal carcinoma were taken as controls, from the department of General Surgery. The cases those were suffering from diabetes mellitus, hypertension and obesity were excluded both from the case and the control group, those conditions which had independent influence on serum lipid levels were not included in this study.

Selection criteria

- Patients from both sexes
- Patients from different age group and diagnosed to have carcinoma of the colon and rectum by clinical methods and different investigations.
- Patients in preoperative stage
- Patients not receiving any previous chemotherapy or radiotherapy

Exclusion criteria

1. Patients suffering from other independent risk factors for serum lipid values such as diabetes mellitus, hypertension and obesity.
2. The cases, whose histology became negative for malignancy, but lipid profile done earlier, were excluded from this study.

Method of selection of cases

Diagnosis of carcinoma of colon is done by a series of clinical examinations as well as by a number of investigative modalities including preoperative colonoscopy, ultra sonogram and FNAC.

Clinical examination

General examination

1. Body built of the patients
2. Lymphadenopathy
3. Presence of jaundice

Per abdominal examination

Inspection – abdominal distension

Visible swelling or visible peristalsis

Palpation - Feeling of a mass in the abdomen

(Mobile or fixed, it's location)

Presence of tenderness is there or not

The presence or absence of ascites

Feeling for hepatomegaly and secondaries in the liver

Per-rectal examination

Feeling of a hard irregular mass in the rectum or may be normal in colonic diseases

Proctoscopy

Visible growth or ulceration

Investigations

1. Ultrasonogram of abdomen and pelvis
(Detection of mass and its location, status of the liver and abdominal lymph nodes, ascites)
2. Colonoscopy and Colonoscopic biopsy and histopathology
3. Contrast helical computerized tomogram scanning of abdomen and pelvis
(To know the local spread of the disease, liver and lymph node status)
4. X-ray of the chest (to know about pulmonary metastasis)
5. Intra operative finding and excisional biopsy and histopathological study

After diagnosis of the cases as colorectal carcinoma, the overnight fasting blood sample of

the patient was collected and sends for lipid profile examination, in the department of Biochemistry of VSS Institute of Medical Science and Research, Burla

The following parameters of serum were estimated:

1. Serum total cholesterol (TC)
2. High- density lipoprotein cholesterol (HDL-C)
3. VLDL – cholesterol (VLDL-C)
4. LDL- cholesterol (LDL-C)
5. Tri-glycerides (TG)

The serum cholesterol was estimated in the department of Biochemistry by Logotech- techno-168 semi-auto analyzer by enzymatic methods. The overnight fasting sample of blood was collected and sent to the department of Biochemistry of VSS Institute of Medical Science and Research, Burla and lipid profile estimation was done.

Aims and Objectives

To study in detail the relationship between serum lipids level and the outcome in colorectal carcinoma and thereby any clue to prevent this malignant disease.

Observation

Table – 1 All the observations were recorded in both sexes of cases taking control group as standard for comparison

Serum Parameters	T-C (mg/dl)	TG (mg/dl)	HDL-C (mg/dl)	VLDL-C (mg/dl)	LDL-C (mg/dl)
Normal Values	<200	<170	>30	<40	<150
Mean \pm 2SD controls	175.35 \pm 42.014	176.68 \pm 55.434	41.75 \pm 16.478	35.85 \pm 11.728	98.25 \pm 43.906
Mean of female Cases	143.08	153.25	42.08	30.67	70.33
Mean of Male cases	141.36	152.04	39.00	30.64	71.86

Table above showed the serum TC, TG, HDL-C, VLDL-C and LDL-C values of both sexes separately. Here, though the serum TC, TG and LDL-C values of both sexes of cases were less than those of the controls, it were not that

significant in any of the sexes, as it remains between two standard deviations of control values and the 'P' value being non-significant. There was also, nearly no difference in these values among both the sexes.

Table 2 Lipid profile comparison of right and left sided colorectal carcinoma in both sexes compared separately with those of the controls

Serum Parameters	T-C (mg/dl)	TG (mg/dl)	HDL-C (mg/dl)	VLDL-C (mg/dl)	LDL-C (mg/dl)
Normal Values	<200	<170	>30	<40	<150
Mean \pm 2SD controls	175.35 \pm 42.014	176.68 \pm 55.434	41.75 \pm 16.478	35.85 \pm 11.728	98.25 \pm 43.906
Mean of cases of advanced stages of right sided Ca	123.36	131.73	40.36	27.09	56.73
Mean of cases of advanced stage cases of Left sided Ca	148.90	160.24	39.76	32.00	76.97

This showed the mean values of serum TC, TG, HDL-C, VLDL C and LDL-C of advanced stage diseases (Dukes' C1 and C2) of right side (Caecum, Ascending colon and Hepatic flexure) and left sided cases (Transverse colon, Descending colon, Sigmoid colon and Rectum) of both sexes. The levels of TC, TG and LDL-C were decreased in both left sided and right sided

diseases of advanced stage cases, but the difference was more marked in right sided cases. but it was only the TC, where the mean level of right sided carcinoma was lower beyond the level of controls with two standard deviations, and the P value being less than 0.05, and was significant But this was not cases in left sided carcinoma.

Table 3 Comparison of lipid profile values of cases of early stage diseases (Dukes, A and B), of both sexes, taken together with those of the controls

Serum Parameters	T-C (mg/dl)	TG (mg/dl)	HDL-C (mg/dl)	VLDL-C (mg/dl)	LDL-C (mg/dl)
Normal Values	<200	<170	>30	<40	<150
Mean \pm 2SD controls	175.35 \pm 42.014	176.68 \pm 55.434	41.75 \pm 16.478	35.85 \pm 11.728	98.25 \pm 43.906
Mean of cases of early stages	170.88	183.63	34.00	36.75	100.13

This showed the mean values of serum TC, TG, HDL-C, VLDL-C and LDL-C of Dukes' A and B stages of colorectal carcinoma of both sexes together. Here, though there was a decrease in the

levels of serum TC and HDL-C, the inverse correlation was not that strong and it did not bear statistical significant and $P > 0.05$.

Table 4 Lipid profile comparison of cases in both sexes of colorectal carcinoma, with advanced stages (Dukes C1 and C2), with those of the controls as a whole

Serum Parameters	T-C (mg/dl)	TG (mg/dl)	HDL-C (mg/dl)	VLDL-C (mg/dl)	LDL-C (mg/dl)
Normal Values	<200	<170	>30	<40	<150
Mean \pm 2SD controls	175.35 \pm 42.014	176.68 \pm 55.434	41.75 \pm 16.478	35.85 \pm 11.728	98.25 \pm 43.906
Mean of cases of higher stages	134.63	144.59	41.41	29.12	64.22

I showed that, the mean values of serum TC, TG and LDL-C cases with advanced stages of colorectal carcinoma. The serum levels of TC and LDL-C in cases were nearly two standard

deviations less than the mean values of controls and $P > 0.05$. but the difference in other serum levels like HDL and VLDL-C were not the significant.

Table 5 lipid profile comparison of all stages of cases of colorectal carcinoma, of both sexes together, with those of controls

Serum Parameters	T-C (mg/dl)	TG (mg/dl)	HDL-C (mg/dl)	VLDL-C (mg/dl)	LDL-C (mg/dl)
Normal Values	<200	<170	>30	<40	<150
Mean \pm 2SD controls	175.35 \pm 42.014	176.68 \pm 55.434	41.75 \pm 16.478	35.85 \pm 11.728	98.25 \pm 43.906
Mean \pm 2SD of cases	141.88 \pm 43.950	152.40 \pm 49.754	39.93 \pm 11.814	30.65 \pm 8.984	71.40 \pm 41.530

It showed the mean values of serum TC, TG and LDL-C of cases were less than those of controls, when taken as a whole and the $P > 0.05$ but it had within two standard deviations of controls, and that was not that significant. The values of HDL-C and LDL-C of cases compared with those of controls as found to be of no significant difference.

Discussion

The comparative analysis of different serum parameters like TC, TG, HDL-C, VLDL-C, and LDL-C were contemplated in all 40 cases of colorectal carcinomas, taken as test cases in its different stages and locations in both males and females. A similar group of 40 other cases who were not having colorectal malignancy was taken as the control. It was observed that, the mean value of total serum cholesterol level in control group was 175.35, in contrast to a value of 141.36 in cases with colorectal malignancies. This showed a lower value of total serum cholesterol in our colorectal carcinoma group, which positively correlates with the findings of Seth R et al (1981), who found that, cases of colorectal carcinoma had lower serum cholesterol values, whereas cases with advanced tumors had significantly lower cholesterol levels than those of the controls.

Similarly, the serum TG and LDL-C values in tumor group were found to be lower than the control group. Here the mean values of TG and LDL-C of controls were 176.68 and 98.25 respectively, against the values of 152.40 and 71.40 respectively in tumor group. Of course, this finding was almost consistent with the observations of Abraham M Y et al (1991), who

stated that, an inverse association between serum cholesterol level and colon malignancy risks coexist, when taking all sub-sites of different parts of colon.

This present finding can also run parallel favoring the findings of MC Michel AJ and Potter JD (1981), who observed that, low cholesterol levels have been associated with increased fecal bile acid concentration in human beings, the bile acids being specifically the deoxycholic acid type, which have been found to produce carcinogenesis on colon in experimental animals.

In our study it was observed that, cases of colorectal carcinoma in late stage of the disease (Dukes C1 and C2) were having lower values of TC and LDL-C. The serum levels of TC and LDL-C in control groups were 175.35 and 98.25 respectively in contrast to values of 134.63 and 64.22 respectively in tumor groups. This finding agreed with the findings of Seth R, et al (1981). But, Seth R, et al, did not include the estimation of LDL-C levels in their study.

In this present study, the TG and VLDL-C levels were decreased but not significant, whereas the mean level of HDL-C was unchanged all throughout.

A data obtained from a WHO trial by "The committee of Principal Investigators" (1978), indicated that lowering serum cholesterol level by use of Clofibrate was associated with a significant spurt in incidence of gastrointestinal malignancy. However in contrary, Ederer F, et al (1980), demonstrated that, reducing serum cholesterol by means of a polyunsaturated fat diet however, showed no increase in incidence of malignancy or mortality due to colorectal carcinoma.

In the present study done in this institution with tumor cases affecting right and left sided colon and rectum, a peculiar finding was observed and was compared with the taken control group. The mean values of total serum cholesterol, triglyceride and LDL-C in right sided tumors (caecum, ascending colon and hepatic flexure) were 123.36, 131.73 and 56.73 respectively, which were seen to be grossly in the lower side than those of the levels in the control group. Of course, these parameters were also decreased in left sided colonic and rectal malignancies, but not significant statistically. So the parameters in the above three group, i.e. right sided and left sided malignancies and control group were totally different. However a standard deviation beyond 2 in this was highly significant in comparing the mean TC levels between the right sided case and the control group. This observation was consistent with the findings of Abraham M Y, et al (1991), who had a strong inverse association between the serum cholesterol levels and colorectal carcinoma risk, as the incidence moved from sigmoid colon to caecum. The postulated that the metabolic effect of undiagnosed colon cancer contributed to this inverse association. But it was rather unclear that, why the association was stronger for caecum, ascending colon cancer and not in case of rectal cancer.

The present series did not find any significant difference in the levels of different serum parameters in the early stage of the malignancy (Dukes' A and B) when compared with the corresponding control group. This finding was similar to the findings of Seth R, et al (1981). In the series of Seth R, et al, in early tumor group this inverse correlation of these serum parameters with those of the controls was not statistically significant.

Sex did not had any influence in alteration of serum parameters evaluated by us in both tumor and control groups. However Abraham M, et al had a low serum cholesterol level proceeding the diagnosis of colon cancer in men and supported his view that, it could be pre-clinical

manifestation of colorectal carcinoma, but in their study the did not include any female cases and also had findings of negative correlation between colorectal carcinoma in men and the levels of serum TC, TG and LDL-C levels which was shown in Table – 1.

Summary and Conclusion

The present piece of work was being attempted in this institution keeping in view the works done by other authors in different setups elsewhere in the world in recent years. Till date, very many authors are in line to postulate some correlation of serum TC, TG and LDL-C with different colonic and rectal malignancies and all these studies are having a comparable control group.

Preoperatively all the cases having doubt of malignancy in colon and rectum were subjected to through clinical examinations and relevant investigations. They had their TC, TG, HDL-C, VLDL-C and LDL-C estimated before surgery. The confirmed cases of colorectal cancers were taken as the group of study. Another, control group, who had no colorectal malignancies and being treated for some other afflictions, was kept for comparison. In the malignant group, the cases were subdivided according to their site of affection and the stage of the disease.

The observation was that, a decrease in serum levels of TC, TG and LDL-C was seen in tumor group as against the levels in the control group irrespective of sex, location and stage of the malignancy. Though there was a meager difference in levels, it was not statistically significant.

But, significant difference was seen in the serum levels of above parameters in advanced cases only comprising Dukes' C1 and C2.

When the serum parameters of cases with right sided carcinomas and left sided carcinomas are compared with those of the controls, it was found that, the mean levels of TC, TG and LDL-C of right sided cases were significantly lower than the left sided carcinomas and the decrease in the level of serum TC was statistically significant. Though

this inverse correlation was also found in left sided malignancies, the relation was not that strong as that of the right sided tumors. The mean levels of serum parameters of early cases when taken together, though the serum TC value was reduced to some extent, it was not significant.

No significant difference was also found in these serum parameters, when cases of both sexes were analyzed separately. In all these comparisons, the values of HDL-C, and VLDL-C varied a little or nearly unchanged in the study groups.

From our findings we conclude that, there lies an inverse correlation between colorectal carcinoma and serum TC, TG and LDL-C levels. It may be utilized for follow-up of treating colorectal carcinoma cases and also a low level of these serum parameters preceding the disease or in early tumors, may be exploited on screening the cases, so that a more curative approach in treating this dreaded disease may be planned. Earlier to that, as our study consists of a small number of participants, it needs further through investigations and a population based cohort study for further clarification of this relationship.

It is almost documented that, there is a negative correlation between the total cholesterol level in blood and advanced malignancy affecting the right sided colon only, but explanation of this is far from conviction. As this particular work is on in different centers till date with much bigger groups, we hope to have a come, when a genetic link can be searched out to this serum cholesterol and colonic malignancy correlation.

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