ASSOCIATION BETWEEN HYPOLIPIDEMIAS AND COLORECTAL CARCINOMA

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ABSTRACT

Objective: To study association of hypolipidemias and primary colorectal carcinoma in population of patients of colorectal carcinoma presenting to Combined Military Hospital (CMH) Rawalpindi.

Study Design: Case control study.

Place and Duration of Study: Oncology department, Combined Military Hospital (CMH), Rawalpindi.
Material and Methods: Forty one treatment naïve patients between ages of 18-75, with histologically confirmed primary colorectal carcinoma were selected and their serum lipid profile was measured after an overnight fast, from Armed Forces Institute of Pathology (AFIP). These levels were compared with 41 controls, selected from healthier population, using an unpaired T test. Frequency and percentages were computed for variables; sex, age and stage at presentation.

Results: Colorectal carcinoma had significant association with triglycerides (p=0.007), total cholesterol (p=0.014) and LDL (p=0.013).

Conclusion: There is an inverse relationship between serum total and LDL cholesterol, and colorectal carcinoma, implying that hypolipidemias may play a role in development of colorectal carcinoma.

Keywords: Colorectal carcinoma, Hypolipidemias, Serum lipid profile.

INTRODUCTION

The world wide annual incidence of colorectal carcinoma is about 917,000 and is the second leading cause of death among all cancers in Western population[1]. Few studies have been done to observe any association between colorectal carcinoma and serum lipid profile in different sets of populations[1,2]. The results have been varying and some studies have shown an increased potential for the disease to metastasize in presence of increased total cholesterol and low density lipoprotein levels[1]. High intake of dietary fats in itself has been hypothesized to be an etiological factor for colorectal carcinoma[3]. The explanation for this association between high dietary intake of fats and colorectal carcinoma is that increased dietary animal fats produce increased amounts of primary bile salts[4]. These bile salts are subsequently degraded to potentially carcinogenic secondary bile salts, by colonic bacteria[4]. Lipids are high energy yielding molecules and serve as energy stores of the human body. They not only form part of cell membrane but also play an important role in performing various functions in the body like cell division and growth and maintaining the cell integrity[5]. Lipids include fats, oils, phospholipids and some other related compounds. Cholesterol and triglycerides are the major forms of lipid molecules which are transported in the body as lipoproteins.

Hyperlipidemias are known to be a risk factor for coronary artery disease[6]. More than 50% of the patients of hyperlipidemias are unaware of having this underlying disorder[7]. A previous study done in patients of colorectal carcinoma in Irish population showed that the mean total cholesterol levels were lower in patients of colorectal carcinoma but the triglycerides were found to be in normal range in this population of patients[4]. Another study done in American population showed no relationship between serum total cholesterol levels and colorectal carcinomas[8]. Thus some studies supported this association between low serum lipid levels and colorectal carcinoma while others did not support this inverse relationship[9-14]. Lower levels of these lipids have also been associated with carcinogenesis

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in various organs of the body especially in oral cancers[5]. However, to date this inverse relationship between serum lipid level and carcinogenesis is not well established[15]. No such epidemiological study has been carried out in Pakistan to analyze the relationship between serum lipid profile and colorectal carcinoma. This study is aimed to analyze relationship between hypolipidemias and primary colorectal carcinoma, in population of patients of colorectal carcinoma presenting to Combined Military Hospital (CMH) Rawalpindi.

MATERIAL AND METHODS

This case control study was conducted in Oncology Department of CMH, Rawalpindi. Forty one patients aged 18-75 years with treatment naïve histologically proven colorectal carcinoma were included as cases. Patients taking lipid lowering drugs or having synchronous or metachronous second malignancy were excluded. The study duration was one year. Forty one controls comprising of healthy population, were selected from relatives of patients undergoing treatment for any other cancer. All selected cases and controls were enrolled into this study after taking written informed consent and after approval of Hospital Ethical Committee. All cases were subjected to stagingwork-up, which included physical examination, radiological examinations; computed tomography (CT) scan of the abdomen / pelvis, chest x-ray and serum carcinoembryonic antigen (CEA). Clinical staging of all cases, based on above investigations was documented using AJCC 7th Edition. All cases and controls were subjected to an overnight fast of at least 10 hours to minimize bias and standardize test results. Serum lipid profile which constituted of serum triglycerides, serum total cholesterol and serum LDL cholesterol, was evaluated for cases and controls, from Armed Forces Institute of Pathology (AFIP). Single laboratory was used to reduce probable bias arising from different laboratories being used for this purpose.

Normal values for measured parameters were taken as:

Serum Triglycerides: 0.4 – 1.6 mmol / L

Table-1: Comparison of lipid profile between cases and controls.

	Cases n = 41	Controls n = 41	*p*-value
TG			
< 1.6mmol / L	24 (58.5%)	12 (29.3%)	0.007
>1.6 mmol / L	17 (41.5%)	29 (70.7%)	
Cholesterol			
< 5.2 mmol / L	37 (90.2%)	32 (78.0%)	0.014
>5.2 mmol / L	4 (9.8%)	9 (22.0%)	
LDL			
< 3.2 mmol / L	41 (100%)	35 (85.4%)	0.013
>3.2 mmol / L	0 (0%)	6 (14.6%)	

Table-2: Comparison of lipid parameters between different stages among cases.

	Stage II (15)	Stage III (21)	Stage IV (5)	*p* -value
Triglyceride (Mean +SD)	1.948 + 1.72095	1.77 + 0.88692	1.302 + 0.22118	0.447
Cholesterol (Mean +SD)	3.702 + 1.1044	3.7681 +1.29051	4.292 + 2.24717	0.127
LDL (Mean +SD)	1.9573 + .57433	1.8519 + .52045	2.07 + 0.68938	0.088

Serum Total Cholesterol: less than 5.2 mmol / L

Serum LDL Cholesterol: less than 3.2 mmol / L

Data analysis was done with SPSS version 15. Mean and Standard Deviation (SD) were calculated for quantitavive variables. Frequency and percentages were computed for qualitative variables. Chi-squared test was used to compare lipid profile between cases and controls. A *p* value less than 0.05 was considered significant.

RESULTS

Out of 41 cases, 5 (12.2%) were females, while 36 (87.8%) were males. Out of the 41 controls, 11(26.8%) were females and 30 (73.2%) were males (*p*=0.081). Mean age at diagnosis was 48.75 months (SD=15.912) in cases while it was 50.04 months (SD=13.385) in controls (*p*=0.692). Cases had lower mean levels of serum triglycerides, serum total cholesterol and serum LDL; than controls. This difference was statistically significant.

Out of 41 cases, 15 had stage II disease, 21 had stage III disease and 5 had stage IV disease. None of the 41 cases had stage I disease. A TNM stage wise analysis using the one way analysis of variance was performed. There was no statistically significant difference in lipid parameters between different stages of the cases. The difference seen between the mean levels of serum lipid levels among the stage groups of cases, was not found to be statistically significant.

DISCUSSION

Epidemiological data indicate a direct correlation between dietary fats and carcinoma of the colorectum[3,16,17]. It is already known that high serum lipid level is positively correlated with coronary artery disease[6]. Thus it is reasonable to believe that populations with increased mortality from coronary artery diseases will have an increased mortality from colorectal carcinoma. Rose et al showed a direct relationship between these two phenomenon and also postulated that high serum lipid levels can serve as a predictor for colorectal carcinoma[18]. Thus, many studies were conducted to prove or disprove this hypothesis. Some studies did show a positive correlation between the two while others showed that there was indeed an inverse relation between serum lipid profile and colorectal carcinoma[4,19].

Lower levels of serum lipid in cases of colorectal carcinoma have been linked with the preclinical effect of carcinoma[8,20]. While some studies have shown that this decrease in serum lipids occurs more than five years before diagnosis of carcinoma[21,22]. This long duration of five years shows that this decrease may not be due to metabolic effects of carcinoma. Also in this study, there is no association between the stage of tumor and the serum lipid levels as per stage wise subset analysis. Had there been an association, there would have been a statistically significant decrease in levels of serum cholesterol, as the stage of disease becomes more advanced. As already mentioned, increased primary bile acids are the consequence of high dietary fat, which act as carcinogenic agents after being converted to secondary bile acids by colonic bacteria[4]. The question arises that how can decrease in serum lipid levels result in increase in the carcinogenic process? This has been explained by the hypothesis that individuals with lower serum cholesterol levels have an increased propensity to secrete bile and thus an increased risk of producing colorectal carcinoma[23]. Thus the carcinogenic effect of increased dietary fats would be more discernable in subjects with tendency of having lower serum cholesterol levels by virtue of an inherently increased conversion rate to bile acids when compared with general population[4]. Here it must be noted, that the carcinogenic effect of secondary bile acids on colon and rectum, has been proven by intra-rectal instillation of these bile acids in rats[24,25].

This Pakistani population based study has shown that the levels of serum triglycerides, serum total cholesterol and serum LDL cholesterol; were lower in cases than in controls. These findings are comparable with findings of another similar study done on Irish population which showed non statistically significant difference for triglycerides but statistically significant differences for total and LDL cholesterols[4]. Thus serum total cholesterol and serum LDL cholesterol levels were lower in both these studies. An extensive literature search was carried out to compare the results of this study with previous local studies, but none was found.

The main shortcoming of this study was that the generalized nutritional status was not taken into consideration which can be a significant confounding factor. This parameter could have been measured by documenting any

history of weight loss which again was based on memory of the patient which could have confounded results. Another reliable method of using serum albumin and retinol binding protein concentration could have been adopted to remove this confounding factor[4].

CONCLUSION

The findings suggest a statistically significant inverse relationship between serum lipid levels and patients of colorectal carcinoma. This association supports the hypothesis that hypocholesterolemia may play an important role in development of colorectal carcinoma.

CONFLICT OF INTEREST

The authors of this study reported no conflict of interest.

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