

Lipid Profile in Oropharyngeal Cancers in Southern India

A. Anuradha^{1,*}, L.K. Veerathu¹, G. Sudhakar¹, S. Kolla², N. Sidhanathi³, R. Kondreddy⁴, S. Shakila⁵ and J.R. Peela⁵

¹Department of Human Genetics, Andhra University, Visakhapatnam, India

²Department of Biochemistry, Andhra Medical College, Visakhapatnam, India

³Department of Medicine, Andhra Medical College, Visakhapatnam, India

⁴Department of Biochemistry, Mamata Medical College, Khammam, India

⁵Department of Biochemistry, Faculty of Medicine, Quest International University Perak, Ipoh, Malaysia

Abstract: *Background:* Oropharyngeal cancers are the most common cancers in India especially among the rural population of North Coastal Andhra Pradesh where people practice reverse smoking and Tobacco chewing. These cancers mostly cause dysphagia and dyspnea compromising on their quality of life. The study was designed to understand and evaluate the pattern of serum lipid profile in patients suffering from Oropharyngeal carcinomas.

Materials and Methods: A total of 60 patients with Oropharyngeal carcinoma starting from oral cavity and extending up to the level of esophagus have been selected from 25 to 70 years of age with a mean age of 45 years from the Department of Radiotherapy, King George Hospital, Visakhapatnam from March 2011 to Aug 2011. A total of 73 healthy controls in the same age group were also selected. All the 60 cases of oropharyngeal cancers were malignant histologically. Serum Lipid profile was done for all cases and the controls after an overnight fast. Serum Total Cholesterol, High density lipoprotein cholesterol, Low density lipoprotein cholesterol and Triglycerides were measured using authentic kit methods and Very Low density lipoprotein cholesterol was calculated from the triglyceride value (using Friedewald's equation).

Results: Cases of oropharyngeal cancer have shown significant decrease in total cholesterol and Low density lipoprotein cholesterol when compared with that of controls (0.006 and 0.005 respectively). Serum triglycerides and Very low density lipoproteins cholesterol also showed a decrease in cases but not significant statistically. However, High density lipoprotein cholesterol was significantly elevated in patients with oropharyngeal cancers when compared with controls ($p=0.005$). The same trend of low cholesterol and low density cholesterol was observed in both males and females, though not significant among females. However, high density cholesterol levels showed significant rise in both males and females.

Conclusion: The present study has shown significant association between serum lipid profile variations and Oropharyngeal cancer.

Keywords: Cholesterol, Triglycerides, carcinoma and Oropharyngeal.

INTRODUCTION

Oropharyngeal cancers are observed commonly in developing rather than in developed countries [1, 2]. it is the eighth most common cancer worldwide, with its prevalence being particularly high among men. Incidence rates for oral cancer range from 1 to 10 cases per 100000 populations in many countries. In south-central Asia, it is third most common cancer. In India, the incidence rate of oral cancer is 12.6 per 100000 population [3].

Tobacco use is a known etiologic factor for development of oral precancerous as well as cancerous lesions [4, 5]. The use of tobacco and excessive alcohol accounts for about 90% of cancers in the oral cavity and the risk increases when tobacco is used in combination with alcohol or areca nut [6].

Furthermore, smokeless tobacco such as tobacco chewing as a cause for cancer has been demonstrated by the International Agency for Research on Cancer [7].

There is an increased incidence of oropharyngeal cancers in the rural population in North Coastal Andhra Pradesh where people practice reverse smoking and tobacco chewing.

Tobacco carcinogens are known to induce generation of free radicals and reactive oxygen species, which are responsible for high rate of oxidation/peroxidation of polyunsaturated fatty acids. This peroxidation further releases peroxide radicals. These peroxide radicals affect essential constituents of the cell membrane and might be one of the leading causative factors for carcinogenesis/tumorigenesis [8].

Lipids constitute one of the key components of the cell membrane and are essential for Numerous biological functions Together with cell growth and

*Address correspondence to this author at the Department of Human Genetics, Andhra University, Visakhapatnam, India; Tel: +919396921913; Fax: 0891-2767574; E-mail: anuau2000@gmail.com

division of normal and malignant tissues. The association of tissue/blood cholesterol levels and various diseases has been studied extensively, especially the role of cholesterol in the pathogenesis of coronary heart disease. Several researchers have also reported the association of plasma/serum lipids and lipoproteins with different cancers [9-12].

In cancerous conditions, the increase in the lipid peroxidation may be a reason for the greater utilization of lipids including total cholesterol, lipoproteins and triglycerides for new membrane biogenesis. Cells derive these lipids from the circulating lipoproteins and degradation of these major lipoprotein fractions can result in lowering of blood lipid levels, which are seen in various cancers [10, 12-14]. Some researchers have also found that low serum cholesterol increases the risk of cancer [15, 16] and associated mortality [17, 18].

An association has been found between changes in circulatory cholesterol levels and breast cancer and colorectal cancer. However, there are very few reports on plasma lipid profile in cancers of the head and neck region. Furthermore, we did not find any reports specific to oropharyngeal cancer. Considering that this cancer is encountered commonly in our hospital, we aimed to evaluate the serum lipid profile of these patients comparing with that of the healthy controls including (i) Total cholesterol (TC), (ii) Low density lipoprotein cholesterol (LDLC), (iii) High density lipoprotein cholesterol (HDL), (iv) Very low density lipoprotein cholesterol (VLDL) and (v) Triglycerides (TG).

MATERIALS AND METHODS

A total of 60 (36 males and 24 females) patients with a histological diagnosis of oropharyngeal carcinoma in the age group of 25 to 70 years with a

mean age of 45 years from the Department of Radiotherapy, King George Hospital, Visakhapatnam were included in present study. The study period ranged from March 2011 to Aug 2011. A total of 73 (61 males and 12 females) healthy individuals with similar baseline characteristics and after clinically ruling out diagnosis of any cancer, were recruited as controls. These cases were categorized according to age, smoking type and site of tumor as shown in Table 1.

Serum lipid profile was performed on all patients after an overnight fast. Total cholesterol (TC) was estimated using the Cholesterol Oxidase Phenol 4-Aminoantipyrine Peroxidase (CHOD-PAP) Method [19, 20]. The GPO-PAP method was used to estimate triglyceride (TG) levels [21]. VLDL-C levels were derived from (TG) levels [22]. High density lipoprotein cholesterol [23] (HDL) and low density lipoprotein cholesterol (LDLC) were estimated using a two-step procedure i.e., (i) precipitation and (ii) enzymatic determination [24].

Statistical analyses were done using Graphpad software and p-Values calculated using student's t-test.

RESULTS

This study has shown a decrease in serum cholesterol levels in cases in comparison with that of the controls and this decrease was significant for the LDLC levels ($p=0.005$) and TC levels ($p=0.006$). Serum TGs and VLDL were also lowered in the cases compared to controls but the change was not statistically significant. However, there was a significant increase in the serum HDL levels in patients with oropharyngeal cancers when compared with controls ($p=0.005$). The results are described in Figure 1 and summarized in Table 2.

Table 1: Frequency Distribution of Cases as Per Age, Smoking Status and Site of Tumor

Sex	Frequency	Smoking	Frequency	Site of tumor	Frequency
Male	36	Non- smokers	11	Oralcavity Tongue	16 2
Females	24	Smokers	22	Pharynx, esophagus head and neck	11 7 5
Total	60	Reverse Smokers	17	Larynx	15
		Tobacco Chewers	10	Paranasal Sinuses Ear	2 2
		Total	60	Total	60

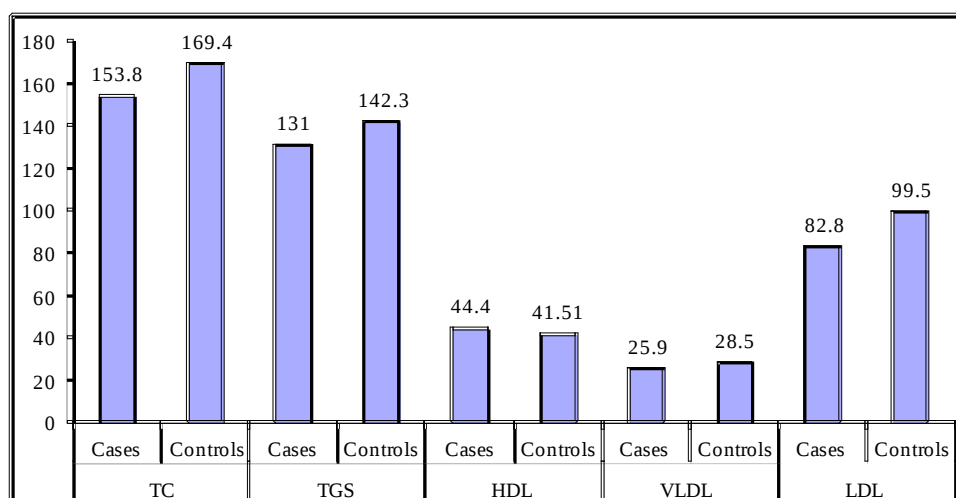


Figure 1: Lipid Profile in Oropharyngeal Carcinomas v/s controls.

Table 2:

Lipids	Type	N	Mean	S.D	t-value	P-value	Decision
TC	Cases	60	153.8	36.7	-2.43	0.006	Significant
	Controls	73	169.4	37.3			
TGS	Cases	100	131.0	67.6	-0.90	0.370	Not Significant
	Controls	73	142.3	76.1			
HDL	Cases	60	44.40	4.16	2.86	0.005	Significant
	Controls	73	41.51	7.33			
VLDL	Cases	60	25.9	13.8	-1.03	0.303	Not Significant
	Controls	73	28.5	15.2			
LDL	Cases	60	82.8	31.1	-2.85	0.005	Significant
	Controls	73	99.5	36.2			

Among males (36cases), there was a significant reduction in the total cholesterol ($p=0.049$) and LDLC ($p=0.016$), whereas TGs ($p=0.127$) and VLDL ($p=0.076$) were decreased but not at a statistically significant level. HDL ($p=0.009$) was significantly increased. These values are summarized in Table 3.

Among females (24 cases VS 12 controls), the same pattern of low TC ($p=0.081$) and LDLC ($p=0.099$) was observed but not significant statistically. TGs ($p=0.401$) and VLDL ($p=0.401$) were also low but not significant. However, the high HDL levels among cases when compared to controls ($p=0.012$) showed statistical significance. These values are summarized in Table 4.

DISCUSSION

Cholesterol and proteins are Vital and integral constituents of the cell, which are essential for various

physiological functions and cholesterol is required for maintenance of the structural and functional integrity of all biological membranes, for the activity of membrane bound enzymes and for stabilization of DNA helix [25].

In some malignancies, serum cholesterol undergoes significant changes early during the disease process, and its levels could be low in the blood as well as tissues because of the process of carcinogenesis [25].

The lower levels of plasma cholesterol and other lipid constituents in patients have been attributed to their increased utilization [26] and one of the postulated mechanisms in cancers caused by tobacco abuse is that there is an increased membrane permeability to carcinogen induced by trans fatty acids [27]. But the findings of alterations in plasma lipid profile in patients with oral precancerous lesions and conditions strongly warrant an in-depth study [28, 29].

Table 3: Males

Lipids	Type	N	Mean	S.D	t-value	P-value	Decision
TC	Controls	61	168.2951	38.64641	2.02	0.049	Significant
	Cases	36	151.6250	32.59343			
TGS	Controls	61	136.0656	62.46409	1.55	0.127	Not Significant
	Cases	36	116.3708	48.31454			
HDL	Controls	61	41.8689	7.74914	-2.68	0.009	Significant
	Cases	36	45.2917	3.93953			
VLDL	Controls	61	27.2459	12.46817	1.81	0.076	Not Significant
	Cases	36	22.4408	10.37943			
LDL	Controls	61	99.1803	38.07953	2.49	0.016	Significant
	Cases	36	79.8004	29.71016			

Table 4: Females

Lipids	Type	N	Mean	S.D	t-value	P-value	Decision
TC	Controls	12	175.2500	30.34985	1.82	0.081	Not Significant
	Cases	24	155.2778	39.53777			
TGS	Controls	12	173.7500	123.67709	0.87	0.401	Not Significant
	Cases	24	140.8222	76.96268			
HDL	Controls	12	39.6667	4.47891	-2.81	0.012	Significant
	Cases	24	43.8056	4.25488			
VLDL	Controls	12	34.7500	24.73542	0.87	0.401	Not Significant
	Cases	24	28.1644	15.39254			
LDL	Controls	12	100.8333	26.23611	1.72	0.099	Not Significant
	Cases	24	84.8356	32.19528			

Alterations of lipid metabolism are already detectable at the time of diagnosis in some paediatric neoplastic patients. The most noteworthy feature being consistently low cholesterol and low HDL cholesterol levels together with hypertriglyceridemia in all paediatric cancer patients with leukaemia and also in Hodgkin's disease [30]. This inverse association between cancer and serum cholesterol may reflect a physiological response to the early stages of malignancy [30].

Several studies have shown an inverse association between blood lipid profile and different cancers [12-14]. Patel *et al.* [25], Schatzkin *et al.* [9] and Chyou *et al.* [31] have reported an inverse trend between serum cholesterol and head neck as well as oesophageal cancers. Many studies have shown a negative correlation of serum cholesterol levels and cancer [32-35]. Owiredo *et al.* demonstrated that in breast cancer

patients, total cholesterol and triglycerides were increased but the HDLC remained unchanged [36]. Our previous study of lipid profile in breast cancer patients in Libya revealed a hike in HDL but there was no fall in levels of TC and LDL [37].

A study of patients with oral cancer, showed a significant decrease in TC, HDLC, VLDLC, and TGs [38]. The possible mechanism for the observed hypolipidemia could be a late change occurring during carcinogenesis which is an effect rather than the cause of cancer. No significant correlation existed between the degree of differentiation in carcinoma, degree of dysplasia in leukoplakia and the serum lipid profile. Tobacco habituates in all forms i.e. Smokeless tobacco and with Smoke showed lower serum lipid levels than non-tobacco users [25]. Moreover, this study shows that tobacco abuse in all forms is deleterious. Undertaking lipid profiling on a larger population of oral

precancer and cancer patients may further strengthen this hypothesis of an inverse relationship between Oropharyngeal Cancers and hypolipidemia [39].

Similarly, in the present study, all lipid parameters were decreased in patients with oropharyngeal cancer, except HDLC, which was significantly elevated compared to the controls.

In a few haematological cancers, decreased LDL < 70mg/dl was associated with fever and sepsis [40]. These varying results on the relationship of serum cholesterol levels to cancer could probably be explained by the performance of the test at different stages of the disease after diagnosis. Some of the limitations of present study are that we did not assess the cholesterol levels of these patients on a long term basis.

In conclusion, present study shows an inverse correlation between serum lipid levels and oropharyngeal cancer, except for serum HDLC levels which has shown an elevation, the mechanism not understood. However, we need larger clinical trials to study the correlation between specific lipid parameters and cancer, and also the mechanisms involved.

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