Alteration of Lipid Profile in Patients with Head and Neck Malignancy

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Abstract Lipids are the major cell membrane components, essential for various biological functions including cell growth and division for the maintenance of cell integrity of normal and malignant tissues. The changes in lipid profile have been associated since long with cancer and hypocholesterolemia has been observed in patients with cancers of various organs. The objective of the present study is to evaluate the alterations and clinical significance of plasma lipid profiles in untreated head and neck malignancies. The present case–control study comprises of newly diagnosed and histologically confirmed, 100 head and neck malignancy cases diagnosed between 1st July 2013 and 30th June 2014 in the Department of Otorhinolaryngology and Head and Neck Surgery, Gandhi Medical College, Bhopal. Fasting blood samples were collected and the lipid profile studied. In present study, the authors found that there is a preponderance of head and neck malignancy in the age group of 41–60 years, males having the higher incidence. Malignancy involving oral cavity were the commonest and majority were well differentiated. Statistically, there was a highly significant reduction of mean serum total cholesterol (TC), triglycerides and high density lipoproteins (HDL) in the subjects of head and neck malignancy as compared to the control group. TC and HDL were also found significantly lower among those with habit of tobacco consumption.

Keywords Lipid profile · Head and neck malignancy · Hypocholesterolemia · Cancer

Introduction

Lipids are major cell membrane components and also the source of energy, essential for various biological functions including cell growth and division of normal and malignant tissues. Usefulness of variations in blood cholesterol levels in diagnosis and treatment of various diseases including cancers has been studied by several workers [9, 11, 17, 20]. Although, its prime role in pathogenesis of coronary heart disease has been consistently found, researchers have reported association of plasma lipids and lipoproteins with different cancers [2, 15, 26]. The alterations in the circulatory cholesterol levels have been found to be associated since long with etiology of breast cancer and colorectal cancer [12, 13]. However, only a few reports are available on plasma lipid profile in head and neck malignancy [8, 24, 26] and in oral cancers in particular [6, 14, 18, 21].

Head and neck malignancy is one of the leading causes of morbidity and mortality, oral cancer predominating [25]. Its incidence is much higher in Asian countries, as compared to the west. The habit of tobacco consumption is a known etiological factor for development of head and neck malignancy [18, 22, 24]. It is believed that tobacco carcinogens 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 which affects essential constituents of the cell membrane [3]. Because of the lipid peroxidation, there is a greater utilization of lipids including total cholesterol (TC), lipoproteins and triglycerides (TG) for new membrane biogenesis.

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Cells fulfill these requirements either from circulation, by synthesis through the metabolism or from degradation of major lipoprotein fractions like LDL, high density lipoproteins (HDL) or very low density lipoproteins (VLDL).

Earlier reports have shown that antioxidant vitamins have protective effects against lipid peroxidation [4, 7, 23]. Lower blood lipids have been associated with various cancers [1, 2, 15]. Furthermore, some investigators have also found the relation of low serum cholesterol with increased risk of cancer occurrence [19, 27], and mortality [5, 10]. The plasma concentrations of lipids are not the single additive function of intake, utilization and biosynthesis because of its continuous cycling in and out of the blood stream. The question that whether hypolipidemia at the time of diagnosis, is a causative factor or is a result of cancer has remained unanswered.

Considering these curiosities, the present study is aimed to evaluate the plasma lipid profile in patients with head and neck malignancy. The association between alterations in plasma lipid profile and habit of tobacco consumption is also being studied.

Methods

The study is a prospective observation carried out on 100 patients of newly diagnosed and histologically confirmed head and neck malignancy, attending the Department of Otorhinolaryngology and Head and Neck Surgery, Gandhi Medical College and Hamidia Hospital, Bhopal (MP), India, between 1st July 2013 and 30th June 2014. Similar observation is also carried out on 50 healthy controls.

Inclusion Criteria

All cases diagnosed clinically as those of head and neck cancer and confirmed by histopathological examination.

Exclusion Criteria

Obese and those with history of hypertension, diabetes mellitus, coronary artery disease, myocardial infarction, patients having any cardiac, renal and hepatic dysfunction and those on chemotherapy and radiotherapy and those on drugs interfering with lipids.

Controls

Age and sex matched subjects who do not have any renal, hepatic or cardiac dysfunction.

The subjects in each group are further classified as with habit of tobacco consumption and without habit of tobacco.

Fasting blood samples are drawn and analysed for lipid profile as recommended in literature.

Results

In present study, among the 100 cases of head and neck malignancy, 68 (68 %) are males and 32 (32 %) are females, male to female ratio being 2.125:1 (Table 1).

In present study, among the 100 cases of head and neck malignancy, the minimum age of presentation is 12 years and maximum 76 years; the majority of cases, 40 (40 %) are in the age group of 41–60 years, followed by 33 (33 %) cases in the age group of 21–40 years, 24 (24 %) cases in group more than 60 years and minimum number of cases i.e., 3 (3 %) below 20 years (Table 2).

In the present study, out of 100 cases of head and neck malignancy, the most common site involved is the oral cavity accounting for 68 % (n = 68) cases followed by 17 % cases involving larynx (n = 17), 11 % in pharynx (n = 11) and maxilla accounting for 4 % (n = 4) cases.

In the oral cavity, buccal mucosa is involved in the majority of cases i.e., 28 % (n = 28) followed by lips accounting for 16 % cases (n = 16), followed by tongue and others accounting for 12 % (n = 12).

In the larynx, the most common site involved is supra-glottis followed by glottis accounting for 16 % (n = 16) and 1 % (n = 10) respectively.

Table 1 Gender distribution

S. no.	Sex	No. of cases of head and neck cancers	Percentage (%)	No. of controls	Percentage (%)
1	M	68	68	28	56
2	F	32	32	22	44
	Total	100	100	50	100

$$\chi^2 = 3.482; df = 2; P = 0.175$$

M males, F females

Table 2 Age distribution

S. no.	Age group (years)	No. of cases	Percentage (%)	No. of controls	Percentage (%)
1	Up to 20	3	3	11	22
2	21–40	33	33	21	42
3	41–60	40	40	18	36
4	>60	24	24	Nil	Nil
	Total	100	100	50	100

Table 3 Site wise distribution

S. no.	Site	Subsites	No. of cases	Percentage (%)
1	Oral cavity	Buccal mucosa	28	28
		Tongue	12	12
		Lips	16	16
		Others	12	12
2	Pharynx	Nasopharynx	2	2
		Oropharynx	9	9
3	Larynx	Supraglottis	16	16
		Glottis	1	1
		Subglottis	–	–
4	Maxilla	–	4	4
		Total	100	100

Table 4 Histopathological grade

S. no.	Histopathological grade	No. of cases	Percentage (%)
1	Well differentiated	45	45
2	Moderately differentiated	38	38
3	Poorly differentiated	9	9
4	Undifferentiated	4	4
5	Others	4	4
	Total	100	100

In the pharynx, majority of cases i.e., 9 % involved oropharynx (n = 9) and 2 % cases (n = 2) are in nasopharynx (Table 3).

In the present study, most head and neck malignancy cases i.e., 84 % (n = 84) are histologically squamous cell carcinoma and remaining are of other types. Forty-five percent (n = 45) of the patients are histopathologically graded as well differentiated, 38 % (n = 38) moderately differentiated, 9 % (n = 9) of the cases with poor differentiation and 4 % (n = 4) are undifferentiated. Four percent cases do not fit in aforementioned grades (Table 4).

The intergroup evaluation of serum lipid profile levels among various grades of differentiation do not show a

significant correlation of serum lipid profile and the degrees of differentiation.

The mean serum lipid profile values of cases with head and neck malignancy and control groups are represented in Table 5. The P values are <0.01 for TC and HDL, suggesting that, statistically, there is a highly significant reduction of mean serum TC and HDL in the subjects of head and neck malignancy as compared to the control group. The TG, LDL and VLDL do not show significant reduction in the subjects of head and neck malignancy as compared to the control group (P > 0.05).

In the present study, out of 100 cases of head and neck malignancies, 90 % are reported to consume tobacco in one form or the other. Tobacco in the form of bidi (country cigarette) smoking is common among the cases reported in about 41 % patients, 24 % have the habit of tobacco chewing and 4 % are with habit of tobacco snuff (oral/nasal) whereas 21 % cases consume tobacco both in chewable as well as smoke form. Habit of snuff is usually observed in the female subjects.

In the present study, in majority of cases of head and neck malignancy, i.e., 55/62 (88.71 %) among smokers, 41/45 (91.2 %) among tobacco chewers and in all four who snuffed tobacco, the use of tobacco is reported to be more than 10 years. 36/62 (58.06 %) of the smokers in have habit of smoking for more than 20 years. While, 29/72 (40.3 %) of the tobacco chewers have habit of chewing for more than 20 years.

The plasma lipid levels are compared between those with habit of tobacco and those without habit of tobacco. The controls consuming tobacco show lower mean plasma lipid levels than the non-consumers.

The plasma lipid levels in tobacco habituates with head and neck malignancy are also compared with the controls. TC levels are found significantly lower in subjects with head and neck malignancy with habit of tobacco (P = 0.02). Likewise, HDL levels are decreased in subjects with habit of tobacco (P = 0.001) as well as significantly low level of HDL (P = 0.012) is found in patients with head and neck malignancy as compared to controls (Table 6).

Table 5 Lipid profile in head and neck cancer versus controls

S. no.	Parameter assessed	Control (n = 50) mean ± SD (mg/dl)	Head and neck cancers cases (n = 100) mean ± SD (mg/dl)	P value
1	TC	193.76 ± 8.95	178.66 ± 12.83	<0.001
2	TG	112.73 ± 10.83	100.76 ± 11.98	0.47
3	HDL	48.42 ± 6.62	40.78 ± 7.68	<0.001
4	LDL	120.49 ± 21.28	117.23 ± 21.12	0.43
5	VLDL	22.56 ± 7.82	23.35 ± 6.74	0.47

P < 0.05 = statistically significant

Table 6 Comparison of lipid profile with habit of tobacco consumption

	TC	TG	HDL	LDL	VLDL
Control without habit of tobacco	206.76 ± 10.78	105.61 ± 12.06	40.32 ± 2.34	122.87 ± 10.72	21.28 ± 3.02
Control with habit of tobacco	191.56 ± 5.48	114.84 ± 11.46	37.26 ± 3.26	99.92 ± 9.34	22.38 ± 3.21
Cancer with habit of tobacco	167.59 ± 4.93	105.57 ± 3.94	28.02 ± 0.82	118.43 ± 5.06	19.11 ± 0.76
A	'P' = 0.02	'P' = NS	'P' = 0.001	'P' = NS	'P' = NS
B	'P' = NS	'P' = NS	'P' = 0.012	'P' = NS	'P' = NS

NS not significant

A control without habit of tobacco versus cancer

B control with habit of tobacco versus cancer

Discussion

In present study, the minimum age of presentation is 12 years and maximum is 76 years; the majority of cases, 40 (40 %) are in the age group of 41–60 years, followed by 33 (33 %) cases in the age group of 21–40 years, 24 (24 %) cases in group more than 60 years and minimum number of cases i.e., 3 (3 %) below 20 years.

Patel et al. found majority of cases in the age group of 30–60 years; Chawda et al. reported maximum head and neck cancer in the age group of 30–75 years [6, 24]. Findings of the present study correlates with these studies as the major number of cases i.e., 73 % are between the age of 21 and 60 years.

In present study, 68 (68 %) are males and 32 (32 %) are females. The male to female ratio is 2.125:1. Patel et al. and Chawda et al. reported maximum cases of head and neck cancers in males with male to female ratio of 1.3:1; 1.14:1 respectively [6, 24]. All studies show male predominance although present study reports much higher male to female ratio.

Male predominance can be associated to the increased incidence of tobacco addiction as compared to females.

In the present study, the most common site involved is oral cavity, the oral cancers accounting for 68 % of total head and neck malignancy cases followed by 17 % cases involving larynx, 11 % in pharynx and maxilla accounting for 4 % cases.

Based on cancer registry data in India, 75,000–80,000 new cases of oral cancers are reported annually and it ranks number one among men [25]. The present study supports the established incidence of oral cancers.

In the present study, most head and neck malignancy cases i.e., 84 % (n = 84) are, histologically, squamous cell carcinoma and remaining are of other types. The observation of the histopathological examination of the 100 head and neck malignancy cases reveals, 45 % of the patients showing well differentiation, 38 % showing moderate differentiation, 9 % of the patients showing poor differentiation and 4 % with undifferentiation.

Patel et al. in their study also reported majority of head and neck cancer to be of squamous cell type (94.6 %). Also major number of cases were moderately differentiated type followed by well differentiated, 46.2 and 34.8 % respectively. Kumar et al. also reported 21/30 i.e., 70 % cases of well differentiated squamous cell carcinoma. The present study findings are in accordance with these studies [18, 24].

The intergroup evaluation of serum lipid profile levels in the present study do not show a significant correlation of serum TC, HDL, LDL, VLDL and TG between the various grades of differentiation.

Kumar et al. in their study found serum TC and HDL to decrease marginally with loss of tumor differentiation, but the finding was not significant statistically. All other parameters, that is, LDL, VLDL and TG showed no correlation with the grade of tumor differentiation [18].

The results of present study are also in accordance with the studies conducted by Patel et al., Lohe et al. and Chawda et al. who found no statistically significant correlation of lipid profile with the grade of tumor differentiation [6, 21, 24].

The mean serum lipid profile values in the present study show P values <0.01 for TC and HDL, suggesting statistically, a significant reduction of mean serum TC and HDL in the head and neck malignancy cases as compared to control group. The TG, LDL and VLDL do not show any significant reduction (P > 0.05).

This is in accordance with various studies which have shown an inverse association between blood lipid profile and head and neck cancers [6, 21, 24].

Cholesterol is an essential constituent of lipoprotein fractions like HDL, LDL and VLDL. Seventy-five percent of the plasma cholesterol is transported in the form of LDL. Body cells sequester cholesterol from the LDL fraction of lipoproteins. LDL receptors are necessary for metabolizing circulating LDL levels and nearly 80 % of the plasma LDLC is cleared by LDL receptors [14, 24]. High activity of LDL receptors attributes for lowering the serum cholesterol levels [14, 24].

There are three main competing hypotheses to explain the inverse association between cholesterol concentrations and the incidence of cancer.

Firstly, lower cholesterol values, even before the manifestation or detection of cancer, may be a result of the cancer process.

Secondly, lower cholesterol values may precede the development of cancer but the association with cancer is secondary, i.e., cholesterol serves as a marker for some other causal set of variables.

Thirdly, lower cholesterol values may precede the development of cancer and may be causally associated with the occurrence of some forms of cancer [17].

HDL levels may be a useful indicator, reflecting the initial changes occurring in neoplastic conditions. HDL levels in patients with head and neck malignancy is significantly decreased as compared to the controls, which is in agreement with the previous studies [6, 24]. TG shows no significant decrease in the present study. Alexopoulos et al. [1] also found a non-significant difference in serum TG between controls and patients while Halton and Patel [15, 24] have observed elevated TG levels in patients with malignancy. Serum LDL and VLDL levels do not reveal any significant difference between the two groups. Similar results for LDL and VLDL were observed in a study conducted by Chawda et al. [6].

Hypocholesterolemia is an additional predictor of cancer and it might be a consequence of disease that is mediated by utilization of cholesterol for membrane biogenesis of the proliferating malignant cells [6, 16, 22].

The summary of this study is presented below.

Study (years)	Results	P value
Patel et al. [24]	Lowered plasma cholesterol and HDL level	TC–0.008 HDL–0.001
Chawda et al. [6]	Significant decrease in HDL level	HDL–0.0005
Present study (2014)	Significant reduction of mean serum TC and HDL	TC < 0.001 HDL < 0.001

In present study, about 90 % of the patients with head and neck malignancy are found to consume tobacco in one form or the other. There is significant reduction in TC and HDL among those with habit of tobacco consumption.

This is in accordance with earlier studies which have shown an inverse relation between cholesterol and tobacco related cancers [24, 26, 27].

Lipid peroxidation is an essential biochemical process that involves the oxidation of polyunsaturated fatty acids, the important components of cell membranes. Tobacco

carcinogens generate reactive oxygen species and lipid peroxides, which result in tissue injury, thus damaging the cellular structural blocks like lipids, proteins, DNA, etc. This process affects essential constituents of cell membranes and might be involved in carcinogenesis/tumorigenesis [21, 24].

Conclusion

Cholesterol and Triglycerides are important lipid constituents of the cell and are essential to carry out several vital physiological functions. In some malignant diseases, blood cholesterol undergoes early and significant changes. Low levels of cholesterol in the proliferating tissues and in blood compartments could be due to the ongoing process of oncogenesis. Earlier studies have reported that hypolipidemia may result due to the direct lipid-lowering effect of tumor cells or some secondary malfunction of the lipid metabolism or secondary to antioxidant vitamins [6, 21, 27].

The results of the present study show evidence of an inverse relationship between the serum lipid profile values of TC, HDL and head and neck malignancy, suggesting that serum lipid profile may be used as a biochemical indicator for initial changes occurring in the neoplastic cells. However, a detailed study of cholesterol carrying lipoprotein transport and the efficiency of the receptor system may help in understanding the underlying mechanisms of regulation of plasma cholesterol concentrations in malignancy. Hence, the present findings strongly warrant an in-depth study of alterations in serum lipid profile patterns in patients with head and neck malignancy.

Conflict of interest The authors declare that they have no conflict of interest.

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