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Original Article

A Diagnostic Role of Plasma Lipid Profile in Patients with Head-and-neck Malignancy

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Abstract

Introduction: Head-and-neck squamous cell cancer is the sixth leading cancer by incidence worldwide. Head-and-neck cancer accounts for 30–40% of all malignant tumors in India and the most common malignant neoplasm is oral squamous cell carcinoma. Usefulness of variations in blood cholesterol levels in diagnosis and treatment of various diseases including cancers has been studied by several researchers.

Aims and Objectives: The aim of the study was to compare the serum lipid profiles of different histological grades of head-and-neck squamous cell carcinoma with that of clinically normal controls and also among the grades of head-and-neck squamous cell carcinoma with that of clinically normal controls and also among the grades of carcinoma.

Materials and Methods: A total of 160 subjects were studied. They were divided into case group (with cancer) and control group (without cancer). Lipid profile was compared between these groups in terms of mean and standard deviation.

Results and Conclusion: The mean difference in the levels of total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglyceride (TG) between the case group and control group was significant in our case study, that is, these lipid parameters were significantly lower in the case group than that of the control group. On receiver operating characteristic curve, TC, HDL, and LDL had shown good inverse relation with cancer versus control group as area under the curve (AUC) was 96%, 89%, and 88%, respectively, whereas TG had fair relation with AUC 70%. The lower plasma lipid status may be a useful indicator for initial changes occurring in 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 cancer.

Key words: Grades of tumor differentiation, Head-and-neck cancer, Lipid profile, Squamous cell carcinoma

INTRODUCTION

The annual incidence of head-and-neck cancers worldwide is more than 550,000 cases with around 300,000 deaths each year. About 90% of all head-and-neck cancers are squamous cell carcinomas (HNSCCs).

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HNSCC is the sixth leading cancer by incidence worldwide.[1,2]

Head-and-neck cancer accounts for 30–40% of all malignant tumors in India and the most common malignant neoplasm is oral squamous cell carcinoma.[3,4]

Most HNSCCs arise in the epithelial lining of the oral cavity, oropharynx, larynx, and hypopharynx.[1] These cancers are strongly associated with certain environmental and lifestyle risk factors such as tobacco and alcohol consumption.[2]

Usefulness of variations in blood cholesterol levels in diagnosis and treatment of various diseases including cancers has been studied by several researchers.[5-8]

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It is believed that tobacco carcinogens induce generation of free radicals and reactive oxygen species responsible for the high rate of oxidation/peroxidation of polyunsaturated fatty acids which affects the cell membrane and are thus involved in carcinogenesis. Because of the lipid peroxidation, there is a greater utilization of lipids for new membrane biogenesis.[9]

Hence, the aim of the study was to compare the serum lipid profiles of different histological grades of head-and-neck squamous cell carcinoma with that of clinically normal controls and also among the grades of head-and-neck squamous cell carcinoma with that of clinically normal controls and also among the grades of carcinoma.

Aims and Objectives

Aim

This study aims to find out plasma lipid profile in head-and-neck malignancy patients.

Objectives

The objectives of the study were as follows:

1. To evaluate the plasma lipid profile including (1) total cholesterol (TC), (2) low-density lipoproteins (LDLs), (3) high-density lipoproteins (HDLs), (4) very LDL (VLDLs), and (5) triglycerides (TGs) in head-and-neck malignancy patients
2. To compare the plasma lipid levels in patients with head-and-neck malignancy and in without malignancy
3. To compare the plasma lipid profile in different histopathological grades of head-and-neck malignancy.

MATERIALS AND METHODS

Study Universe

All patients attending the Department of Otorhinolaryngology and Head and Neck Surgery, Sawai Man Singh Hospital, Jaipur.

Study Place

The present study was conducted on outdoor and indoor patients in the Department of Otorhinolaryngology and Head and Neck Surgery, Sawai Man Singh Hospital, Jaipur.

Study Period

The study period was from July 2019 to September 2020.

Study Design

This was a cross-sectional study.

Type of Study

This was a hospital-based descriptive study.

Methodology

These study subjects were divided into two groups.

Group I

Between July 2019 and September 2020, 80 patients presenting with histopathologically confirmed head-and-neck malignancy in the ENT and head-and-neck cancer department of our hospital, a tertiary care referral, were enrolled in the study.

Group II

Control group comprised age- and sex-matched healthy subjects who had no complaint or history of any major illness in recent past and belonged to the similar socioeconomic group as head-and-neck cancer patients.

Histopathologically, head-and-neck malignancy was divided on the basis of their degree of differentiation:

1. Well differentiated
2. Moderately differentiated
3. Poorly differentiated
4. Undifferentiated.

The pathologist from the Department of Pathology of the Sawai Man Singh Medical College, Jaipur, performed the histopathological grading in head-and-neck cancer.

Outcome variable: Following parameters were noted in the patients:

1. TC
2. HDLs
3. VLDLs
4. LDLs
5. TG.

Outcome Analysis

1. Qualitative data were expressed as rate and proportions while quantitative data were expressed as mean and standard deviation
2. Appropriate statistical test was applied as per data yield
3. $P < 0.05$ was taken as statistically significant
4. Low cutoff value drawn by receiver operating characteristic (ROC) curve.

OBSERVATIONS AND RESULTS

The present study was conducted at the Department of ENT and Head and Neck Surgery, Sawai Man Singh Medical College, Jaipur, from July 2019 to September 2020. The aim of the study was to find out plasma lipid profile in head-and-neck malignancy patients. A total number of patients included in this study were 160, these patients were divided into two groups, 80 patients in the case study group and 80 patients in the control group.

The mean age in all 160 patients irrespective of group was 45.29 years, in the case group was 46.00 years and control

group, it was 44.58 years. The percentage of male and female was 90% and 10% in each group. Hence, in a study population, majority of patients were male. It was observed that the oral cavity (71.25%) was the most common site of malignancy followed by larynx (18.75%) and pharynx (10%) in our study [Table 1].

We observed that maximum of patients in our study had tobacco chewing habit 39 (48.75%) followed by smoking 24 (30%). Five cases were related with both tobacco chewing and smoking. Only 4 cases (5%) with head-and-neck malignancy patients had no habits [Figure 1].

TC level and LDL levels were found significantly lower in head-and-neck malignancy cases who had habit of smoking or chewing tobacco product in comparison to cases with no habit of smoking or chewing tobacco, *P*-value was found statistically significant ($P \leq 0.001$ and $P = 0.004$, respectively) [Table 2].

Most of our study cases presented with well-differentiated squamous cell carcinoma grade of tumor (50%) followed by moderately differentiated squamous cell carcinoma (35%) and only 8 (10%) had poorly differentiated squamous cell carcinoma grade of tumor [Figure 2]. The intergroup evaluation of serum lipid profile levels among various grades of differentiation did not show a significant correlation of serum lipid profile and the degrees of differentiation [Table 3].

In our case study, the mean difference of 80.61 mg/dl in TC level was found which was statistically significant (case group vs. control group – 96.94 ± 25.07 mg/dl vs. 177.55 ± 32.57 mg/dl) [Table 4]. Similarly in HDL, the mean difference of 18.82 mg/dl in the case group versus control group (36.81 ± 9.64 mg/dl vs. 55.63 ± 10.89 mg/dl) [Table 5], the mean difference of 39.94 mg/dl in LDL (55.45 ± 21.41 mg/dl vs. 95.39 ± 26.48 mg/dl) [Table 6], and the mean difference in TG level of 33.28 mg/dl (88.51 ± 21.99 mg/dl vs. 121.79 ± 50.8 mg/dl) [Table 7] were found statistically significant except VLDL with the mean difference of 2.93 mg/dl (21.93 ± 9.64 mg/dl vs. 24.86 ± 11.22 mg/dl) was not statistically significant ($P = 0.078$) [Table 8].

On ROC curve, the maximum area under the curve (AUC) was covered by TC (96%) and the minimum AUC was covered by VLDL (58%) [Table 9 and Graph 1].

Table 1: Distribution according to site of tumor

Site of tumor	*n*	%
Oral cavity	57	71.25
Larynx	15	18.75
Pharynx	8	10
Total	80	100.00

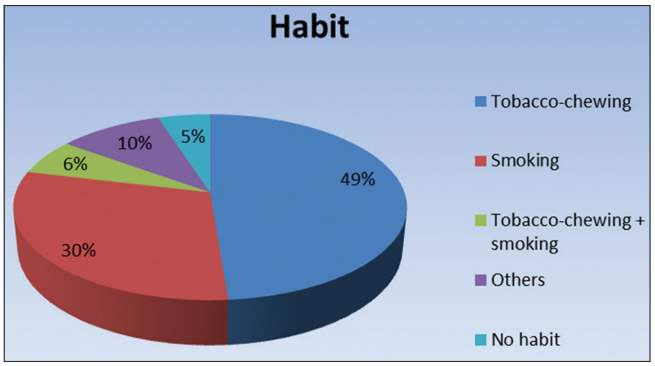


Figure 1: Distribution of study cases according to patients' habits

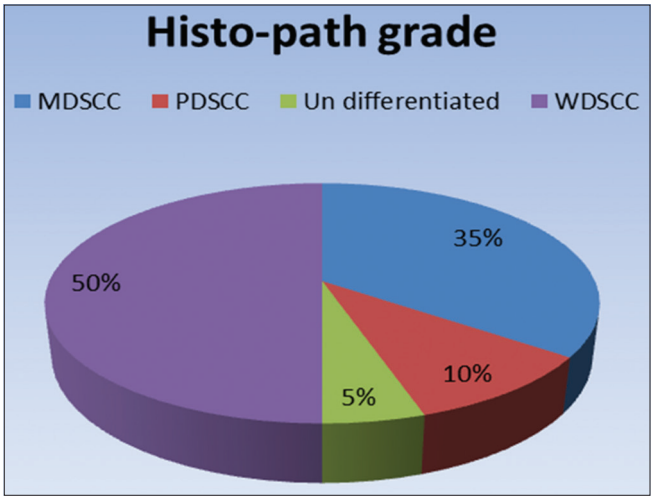


Figure 2: Distribution of cases according to histopathological grade

Low cutoff value for acceptable sensitivity and specificity was calculated and was found for TC – 135 mg/dl (sensitivity 95% and specificity 90%), HDL – 45 mg/dl (sensitivity 83% and specificity 82%), and LDL – 75 mg/dl (sensitivity 82% and specificity 82%) [Table 10].

DISCUSSION

Several authors propose that hypocholesterolemia is a predisposing factor for cancer development. We studied HNSCC cases and compared the serum lipid profile over multiple factors.

Kumar *et al.*[10] 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.[10] The results of the present study were also similar with the studies conducted by Patel *et al.*,[11] Lohe *et al.*,[12] and Chawda *et al.*[13] who found no statistically significant correlation of lipid profile with the grade of tumor differentiation.

Table 2: Correlation of serum lipid profile level with tobacco chewing and smoking habit

Lipid profile	T. chewer		Smoke		Chewer+smoking		Others		No habit		*P*-value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
TC	80.58	20.92	104.56	24.61	99.80	14.97	93.38	22.37	124.25	11.03	<0.001
HDL	35.67	7.90	37.67	10.53	38.80	8.76	33.25	9.54	40.00	13.24	0.675
LDL	42.79	15.69	59.90	19.00	66.40	23.22	55.63	15.19	74.00	46.47	0.004
VLDL	23.54	13.29	20.79	6.98	22.00	7.48	21.88	10.79	23.25	9.39	0.870
TG	89.58	19.53	88.97	22.90	87.60	18.19	80.38	21.06	95.00	37.90	0.830

TC: Total cholesterol, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, TG: Triglyceride, VLDL: Very low-density lipoprotein

Table 3: Correlation of serum lipid profile levels among various grades of differentiation

Lipid profile	WDSCC		MDSCC		PDSCC		Undifferentiated		*P*-value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
TC	93.58	23.65	102.61	23.48	88.38	26.91	108.00	42.68	0.280
HDL	38.40	10.30	37.11	8.77	29.00	5.88	34.50	9.54	0.083
LDL	55.93	23.74	55.68	19.78	52.25	18.10	55.50	20.82	0.978
VLDL	20.95	7.51	21.50	10.37	25.88	14.63	26.75	12.53	0.428
TG	87.68	21.68	87.07	23.93	94.38	15.85	95.25	26.37	0.778

TC: Total cholesterol, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, TG: Triglyceride, VLDL: Very low-density lipoprotein, WDSCC: Well-differentiated squamous cell carcinoma, MDSCC: Moderately differentiated squamous cell carcinoma, PDSCC: Poorly differentiated squamous cell carcinoma

Table 4: Distribution of subjects according to TC level

	TC						
Group	*n*	Mean	SD	Median	Minimum	Maximum	*P*-value
Case	80	96.94	25.07	98.00	44	170	<0.001
Control	80	177.55	32.57	177.50	97	260	
Total	160	137.24	49.74	132.00	44	260	

TC: Total cholesterol

Table 5: Distribution of subjects according to HDL level

	HDL						
Group	*n*	Mean	SD	Median	Minimum	Maximum	*P*-value
Case	80	36.81	9.64	35.00	17	68	<0.001
Control	80	55.63	10.89	56.50	27	77	
Total	160	46.22	13.93	45.00	17	77	

HDL: High-density lipoprotein

Table 6: Distribution of study subject according to LDL level

	LDL						
Group	*n*	Mean	SD	Median	Minimum	Maximum	*P*-value
Case	80	55.45	21.41	54.00	13	138	<0.001
Control	80	95.39	26.48	95.00	13	167	
Total	160	75.42	31.26	75.00	13	167	

LDL: Low-density lipoprotein

Table 7: Distribution of study subject according to TG level

	TG						
Group	*n*	Mean	SD	Median	Minimum	Maximum	*P*-value
Case	80	88.51	21.99	91.50	43	146	<0.001
Control	80	121.79	50.89	110.00	43	288	
Total	160	105.15	42.49	99.00	43	288	

TG: Triglyceride

In our present study, the majority of the cases of head-and-neck cancer group had habit of tobacco. The mean serum lipid profile level of TC, HDL, LDL, VLDL, and TG, between head-and-neck cancer no habit tobacco and who habit tobacco, was compared, there was significant difference found in mean HDL and LDL levels ($P < 0.001$ and 0.004, respectively).

The mean difference in the levels of TC, HDL, LDL, and TG between the case group and control group was significant in our case study, that is, these lipid parameters were significantly lower in the case group than that of the control group. However, the mean difference in VLDL levels was not statistically significant. Lohe *et al*.[12] also found similar observations of the serum lipid profile that there was significant decrease in TC, HDL, VLDL, and TG in oral cancer group as compared with the control group.

On ROC curve, TC, HDL, and LDL had shown good inverse relation with cancer versus control group as AUC was 96%, 89%, and 88%, respectively, whereas TG had fair relation with AUC 70%.

Our results added to this evidence of an inverse relationship between lower plasma lipid profile and head-and-neck malignancies. This was in accordance with various studies

Table 8: Distribution of study subject according to VLDL level

	VLDL						
Group	***n***	**Mean**	**SD**	**Median**	**Minimum**	**Maximum**	***P*-value**
Case	80	21.93	9.64	21.00	9	59	0.078
Control	80	24.86	11.22	22.00	9	63	
Total	160	23.39	10.53	21.00	9	63	

VLDL: Very low-density lipoprotein

Table 9: AUC

Test result variable (s)	AUC	Std. error (a)	Asymptotic sig. (b)	Asymptotic 95% confidence interval	
				Lower bound	Upper bound
TC	0.968	0.012	0.000	0.944	0.992
HDL	0.894	0.026	0.000	0.844	0.945
LDL	0.888	0.028	0.000	0.834	0.942
VLDL	0.580	0.045	0.082	0.491	0.668
TG	0.705	0.042	0.000	0.623	0.787

TC: Total cholesterol, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, TG: Triglyceride, VLDL: Very low-density lipoprotein, AUC: Area under the curve

Table 10: Coordinates of the curve

Test result variable (s)	Positive if ≤ (a) (mg/dl)	Sensitivity	1-specificity
TC	135.50	0.950	0.100
HDL	45.50	0.838	0.188
LDL	75.50	0.825	0.188
VLDL	21.50	0.613	0.488
TG	99.50	0.638	0.375

TC: Total cholesterol, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, TG: Triglyceride, VLDL: Very low-density lipoprotein

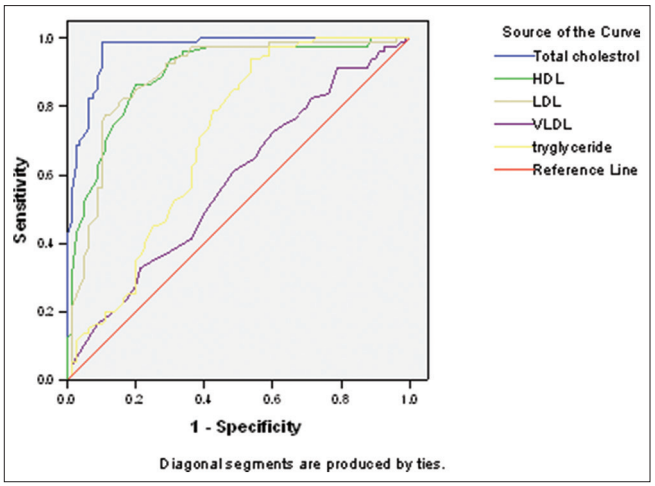
which had shown an inverse association between blood lipid profile and head-and-neck cancers.[14-16]

There are three main competing hypotheses to explain the inverse association between cholesterol concentrations and the incidence of cancer. First, lower cholesterol values, even before the manifestation or detection of cancer, may be a result of the cancer process.

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

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

The lower plasma lipid status may be a useful indicator for initial changes occurring in 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



Graph 1: Receiver operating characteristic curve

of plasma cholesterol concentrations in cancer. In our study, we found that altered lipid profile was associated with head-and-neck malignancies.

SUMMARY AND CONCLUSION

Cholesterol and TGs 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. The results of the present study showed evidence of an inverse relationship between the serum lipid profile 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.

ETHICAL APPROVAL

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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