

Original Research

Study Of Alteration Of Serum Lipid Profile In Patients With Oral Malignancy At A Tertiary Hospital

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ABSTRACT

Background: Among all oral malignancies, the most common malignancy contributing to about 90% is oral squamous cell carcinoma (OSCC). The alterations in the circulatory cholesterol levels have been found to be associated with head and neck cancers. Present study was aimed to evaluate alterations in plasma lipid profile in oral cancer patients and its association with histological grading. **Material and Methods:** Present study was a prospective cross sectional study, conducted in patients with malignancy, lesions diagnosed on the basis of histopathological examination were considered as cases. Age & gender matched, healthy volunteers were taken as control. **Results:** In present study, 40 cases & 40 controls were studied. Majority of cases were from 41-50 years (35 %) & 31-40 years (32.5 %), were male (87.5 %), had history of alcohol consumption (67.5 %) & had history of tobacco consumption (67.5 %). In present study, majority had primary site of involvement as tongue (37.5 %) & buccal mucosa (22.5%), majority were stage III (47.5 %) & stage I (20 %), as per histopathological grading as well differentiated (57.5 %) & moderately differentiated (35 %). We compared various lipid levels (Cholesterol, TG, HDL, LDL & VLDL) among cases & controls. Levels of Cholesterol, TG, HDL & LDL were lowest in patients with oral malignancies as compared to healthy controls & difference was statistically significant ($P < 0.05$). In present study, various lipid levels (Cholesterol, TG, HDL, LDL & VLDL) among various histopathological grading (well differentiated, moderately differentiated & poorly differentiated) oral malignancies were comparable & difference was statistically not significant ($p > 0.05$). **Conclusion:** The lower levels of plasma cholesterol and other lipid constituents in patients might be due to their increased utilization by neoplastic cells for new membrane biogenesis.

Keywords: Plasma cholesterol, plasma lipid profile, oral malignancy, tobacco consumption

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INTRODUCTION

Among all oral malignancies, the most common malignancy contributing to about 90% is oral squamous cell carcinoma (OSCC).¹ Not only OSCC but also the use of tobacco and arecanut can also lead to potentially malignant disorders.² The high incidence of OC and oral precancerous lesions in India has been linked with the traditional habit of betel quid chewing incorporating tobacco. Men are affected by two to three times more as compared to women.³

Squamous cell carcinoma of the oral cavity is responsible for considerable morbidity and mortality in India, where 60,000 new cases of oral cancer are reported to occur every year.⁴ Oral cavity cancer is currently the most frequent cause of cancer related deaths among Indian men, which is usually preceded by oral potentially malignant disorders like oral leukoplakia (OL) and/or oral submucous fibrosis (OSMF).⁵

Lipids play an important role in maintaining the cell membrane integrity. Lipid profile is a panel of blood tests that serve as an initial medical screening for abnormalities in lipids and approximate risk for cancer, cardiovascular diseases, pancreatitis, etc., Researchers have reported association of plasma/serum lipids and lipoproteins with different cancers. The alterations in the circulatory cholesterol levels have been found to be associated with head and neck cancers.^{6,7} Present study was aimed to evaluate alterations in plasma lipid profile in oral cancer patients and its association with histological grading.

MATERIAL AND METHODS

Present study was a prospective cross sectional study, conducted in department of Department of ENT and Head, Neck Surgery, at B.K.L. Walawalkar Rural Medical College & Hospital, Sawarde, Chiplun, Ratnagiri, India. Study duration was of 2 years (July 2019 to June 2021). Study was approved by institutional ethical committee.

Inclusion criteria: All patients with malignancy, lesions diagnosed on the basis of histopathological examination were considered as cases. Age & gender matched, healthy volunteers were taken as control

Exclusion criteria: Those patients who were non-compliant, had prior treatment history with surgery, radiation or chemotherapy, Patients having co-morbid illnesses such as diabetes, obesity, hypertension, anemia, jaundice, liver or kidney disorders or any other systemic diseases as well as malignancies detected elsewhere in the body and Patients currently taking drugs that alter the lipid levels

Study was explained to patients & written informed consent was taken for participation. A comprehensive history was carefully obtained with special reference to their tobacco habits, its nature, duration and frequency of use, followed by detailed physical examination and clinical staging. All patients underwent routine blood investigations along with plasma lipid profile.

Fasting blood samples were collected from the subjects, into EDTA containing vacuettes. Serum total cholesterol, HDL, TG, LDL was estimated by using semi-automated chemical analyser using colorimetric method (Selectra Pro M, ELITech Group-Biomedical Systems Division, USA) with the help of reagent (Q line, POCT Services Private Limited, New Delhi, India).

Lipid profile with following range were used.

Total cholesterol: - borderline high -200-239 mg/dl; high- \geq 240 mg/dl;

TG:- borderline high- 150-199 mg/dl; high- 200-499 mg/dl;

HDL:- low <40 mg/dl; high >60 mg/dl;

LDL:- high >150 mg/dl)

Various radiological (chest x-ray, CT/MRI head and neck and USG abdomen), histopathological (incisional biopsy of mucosal lesion) investigations, findings of fiberoptic nasal and laryngeal endoscopic examination and FNAC of cervical lymph nodes were performed wherever indicated.

Patients were further staged according to TNM staging of oral tumors (AJCC Cancer Staging Manual). These patients were categorized into 3 groups according to the degree of differentiation on the basis of histopathology:

Group 1: Highly Differentiated OSCC;

Group 2: Moderately differentiated OSCC;

Group 3: Poorly differentiated OSCC;

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. The results were analyzed in mean, standard deviation (SD) and percentages. The lipid levels were compared by using unpaired t-test between two strata. The $p < 0.05$ was considered significant.

RESULTS

In present study, 40 cases & 40 controls were studied. Majority of cases were from 41-50 years (35 %) & 31-40 years (32.5 %), were male (87.5 %), had history of alcohol consumption (67.5 %) & had history of tobacco consumption (67.5 %).

Table 1: General characteristics

Parameters	No. of cases (N=40)	Percentage (%)
Age (in years)		
<30	2	5.00%
31-40	13	32.50%
41-50	14	35.00%
51-60	6	15.00%
>60	5	12.50%
Mean \pm SD (years)	46.47 \pm 11.14	
Gender		
Male	35	87.50%
Female	5	12.50%
Other		
Family history of cancer in first degree relative	2	5.00%
Alcohol consumption	27	67.50%
Tobacco habit		
Chewing	27	67.50%
Smoking	18	45.00%
Both	13	32.50%
Absent	11	27.50%

In present study, majority had primary site of involvement as tongue (37.5 %) & buccal mucosa (22.5%), majority were stage III (47.5 %) & stage I (20 %), as per histopathological grading as well differentiated (57.5 %) & moderately differentiated (35 %).

Table 2: Characteristics of oral malignancies

Parameters	No. of cases (N=40)	Percentage (%)
Site of involvement		
Tongue	15	37.50%
Buccal mucosa	9	22.50%
Gums	6	15.00%
Lower lip	3	7.50%
Hard palate	3	7.50%
Retro molar trigone	2	5.00%
Upper lip	1	2.50%
Floor of mouth	1	2.50%
Staging of cancer		
Stage I	8	20.00%

Stage II	7	17.50%
Stage III	19	47.50%
Stage IV	6	15.00%
Histopathological grading		
Well differentiated	23	57.50%
Moderately differentiated	14	35.00%
Poorly differentiated	3	7.50%

We compared various lipid levels (Cholesterol, TG, HDL, LDL & VLDL) among cases & controls. Levels of Cholesterol, TG, HDL & LDL were lowest in patients with oral malignancies as compared to healthy controls & difference was statistically significant ($P < 0.05$).

Table 3: Assessment of lipid profile in both the groups

Lipids levels (Mean \pm SD)	Cases (oral malignancy)	Controls	P value
Cholesterol	144.91 \pm 32.45	178.22 \pm 29.59	0.045
HDL	38.94 \pm 8.21	55.6 \pm 11.67	0.022
Triglyceride	96.16 \pm 55.94	148.2 \pm 48.62	0.012
LDL	98.17 \pm 23.82	140.6 \pm 38.75	0.010
VLDL	19.5 \pm 8.24	22.51 \pm 11.21	0.092

In present study, various lipid levels (Cholesterol, TG, HDL, LDL & VLDL) among various histopathological grading (well differentiated, moderately differentiated & poorly differentiated) oral malignancies were comparable & difference was statistically not significant ($p > 0.05$).

Table 4: Comparison of lipid levels among different Histopathological grading.

Histopathological grading	Cholesterol	TG	HDL	LDL	VLDL
Well differentiated	148.72 \pm 31.23	98.87 \pm 51.22	43.21 \pm 12.28	101.18 \pm 32.13	21.18 \pm 5.13
Moderately differentiated	139.33 \pm 24.03	81.50 \pm 51.53	39.52 \pm 11.03	93.92 \pm 30.91	16.92 \pm 3.71
Poorly differentiated	128.62 \pm 29.34	53.03 \pm 29.72	32.41 \pm 8.72	82.73 \pm 22.73	12.73 \pm 2.43
P value	0.19	0.29	0.81	0.87	0.72

DISCUSSION

Phospholipids and cholesterol have been reported to undergo early and significant changes in certain types of malignant tumors. The process of carcinogenesis could be responsible for low levels of cholesterol in the proliferating tissues and in the blood compartments.⁶ However, 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.^{6,8}

Ghosh G et al.,⁹ noted a significant decrease in serum total cholesterol (TC) levels, triglyceride levels ($p = 0.007$, $p = 0.029$ respectively) were observed in oral squamous cell carcinoma patients as compared to the healthy control group. The mean serum HDLC levels ($p = 0.003$) were significantly lowered in the tobacco habituates when compared to the healthy controls. The mean serum total cholesterol levels were significantly lower in subjects with oral squamous cell carcinoma ($p = 0.000$) as compared to the tobacco habituates. Likewise, LDLC levels and TC:HDLC ratios ($p = 0.000$ and $p = 0.000$ respectively) were significantly decreased in oral squamous cell carcinoma patients as compared to the tobacco

habituates. The lower level of serum cholesterol and other lipid constituents in the patients is thought to be due to their increased usage by tumor cells for new membrane biogenesis.

Chawda JG et al.,¹⁰ studied 25 oral cancer patients and 5 controls, levels of total lipids, cholesterol and HDL were significantly lower in oral cancer patients as compared to controls, but LDL and VLDL values were not significant. An inverse relationship was found between the lipid levels and the occurrence of oral cancer. Hence, the lower plasma lipid status may be a useful indicator to detect the initial changes seen in neoplastic process.

Singh M et al.,¹¹ studied 150 consecutive patients of oral squamous cell carcinoma (OSCC) and its oral pre-cancerous (OPC) lesions. Total cholesterol, TG, HDL, and LDL were significantly reduced in OSCC and OPC groups when compared with the reference values. Serum TC, LDL and HDL levels were found to be decreased with the loss of differentiation in histological grading but with no statistical significance. There was an inverse relationship between the serum lipid profile values of TC, HDLC, TG, LDL and OSCC as well as OPC patients. The lower serum lipid status may be considered a useful indicator for initial changes occurring in neoplastic cells.

In study by Rai V et al.,¹² out of 25 patients, males were 18 and females were 07. The mean cholesterol in OSCC patients was 143.7mg/dl and in control was 180.2 mg/dl, HDL was 37.8 mg/dl in OSCC and 55.6 mg/dl in control, triglycerides was 105.2 mg/dl in OSCC and 148.2 mg/dl in control. LDL was 105.4 mg/dl in OSCC and 140.6 mg/dl in control. VLDL was 24.5 mg/dl in OSCC and 23.5 mg/dl in control. The difference was significant ($P < 0.05$).

Vyas T et al.,¹³ noted an overall declining level in percentage deviation of each lipid parameters from non-oral cancer patient group to oral cancer patient cases has been observed to be higher (22%) for Trg parameter, followed by their intermediate values of 20% in VLDL, 18% in LDL, 16% in TC and their recorded lowest value of only 7% in HDL parameter. Furthermore, reduction in all such chosen lipid profile parameters, except in the case of the HDL, in oral cancer patient category relative to non-oral cancer patient cases was found the best statistical significance levels. The lower plasma lipid status may be a useful bio-marker indicator for initial changes occurring in neoplastic cells.

Smoking tends to increase blood cholesterol levels. Furthermore, the ratio of high-density lipoprotein (HDL) (the “good” cholesterol) to low-density lipoprotein (LDL) (the “bad” cholesterol) tends to be lower in smokers compared to nonsmokers.¹⁴ Tobacco carcinogens induce generation of free radicals and reactive oxygen species which are responsible for the high rate of peroxidation of polyunsaturated fatty acids. This affects essential constituents of the cell membrane and may be involved in carcinogenesis. Lipid peroxidation leads to greater utilization of lipids, including total cholesterol, lipoproteins and triglycerides for new membrane biogenesis. Lower lipid profile levels have been associated in a variety of cancers ranging from head and neck to pancreatic cancers.¹⁵

The main hallmark of cancer is uncontrolled and unwanted proliferation of cells leading to tumor formation. The cell membrane is made up of lipoproteins. Thus, the body lipids are used for the biogenesis of the cell membranes of the newly forming neoplastic cells and this causes a decrease in the cholesterols, TGs, and lipoproteins in the cancer patients.

The change in lipid levels may have a diagnostic or prognostic role in the early diagnosis or prognostication of oral premalignant and malignant lesions. The findings strongly warrant an in-depth study of alterations in plasma lipid profile in these patients.

CONCLUSION

The lower levels of plasma cholesterol and other lipid constituents in patients might be due to their increased utilization by neoplastic cells for new membrane biogenesis. The

findings strongly warrant an in-depth study of alterations in plasma lipid profile in head neck cancer patients.

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