Original Article

Alterations in serum lipid profile patterns in oral cancer

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Abstract

Background: Alterations in serum lipids have long been associated with cancer as lipids play an important role in maintenance of cell integrity. **Aims:** To evaluate alterations in plasma lipid profile in oral cancer patients, to compare and correlate the serum lipid profile in different grades of carcinoma and to evaluate the correlation of serum lipid profile between the tobacco habituates and non-habituates. **Materials and Methods:** Among 75 study subjects, 50 individuals were oral carcinoma patients and 25 individuals were healthy controls. The parameters assessed included total cholesterol (TC), high-density lipoprotein-cholesterol (HDLC), low-density lipoprotein-cholesterol, very low-density lipoprotein-cholesterol and triglycerides (TGL). These groups were subdivided into subjects with no habit of tobacco (NHT) and subjects with habit of tobacco (WHT). **Stastical Analysis Used:** Evaluation of results and statistical analysis was carried out using Student's *t*-test and one-way Analysis of Variance. **Results:** There was a significant decrease in TC, HDLC and TGL in the oral cancer group as compared with the control group. The lipid profile levels between histological grading of the oral cancer and between WHT and NHT had no statistical significance. **Conclusions:** There was an inverse relationship between serum lipid profile and oral cancer. The lower serum lipid status may be considered a useful indicator for initial changes occurring in the neoplastic cells.

Key words: Histological grades, lipids, oral cancer, tobacco abuse

INTRODUCTION

Lipids are cell membrane components essential for various biological functions. Although their prime role in pathogenesis of cardiovascular disease has been consistently found, researchers have reported an association of serum lipids with different cancers.[1-7] However, only a few reports are available on plasma lipid profile in head and neck cancers.[1,5,7,8] The question of whether hypolipidemia at the time of diagnosis is a causative factor or a result of cancer has remained unanswered.[5] Considering these lacunae, the present study was undertaken to evaluate alterations in plasma lipid profile in oral cancer patients and its association with histological grading and tobacco abuse.

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MATERIALS AND METHODS

The Institutional Ethical Committee approved this study. A total of 75 study subjects were selected. Of these, 50 individuals were histopathologically confirmed oral squamous cell carcinoma patients and 25 individuals were healthy controls, who had no complaint or any major illness in the recent past. Among the cancer patients, 14 subjects had well-differentiated, 27 subjects had moderately differentiated and nine subjects had poorly differentiated carcinoma. The subjects in each group were further classified as having no habit of tobacco consumption (NHT) and with habit of tobacco consumption (WHT). Patients having malignancy other than squamous cell carcinoma and patients with past or present history of treatment for oral squamous cell carcinoma were not included as part of the carcinoma study group.

After taking thorough case history, prior informed written consent and clinical examination of the oral cavity of the same patients, a fasting blood sample was drawn from the antecubital vein with minimal trauma under aseptic conditions. The plasma was separated by centrifugation and the supernatant was separated and analyzed.

The lipid profile was estimated using kits obtained from ERBA diagnostics (Transasia Bio-Medicals Ltd., Mumbai, India). Lipid analysis was done on a chemical analyzer (Erba Chem-5 plus v2 analyzer-Transasia Bio-Medicals Ltd., Mumbai, India) based on the spectrophotometric principle. By using an ultra violet (UV) – visible spectrophotometer, the serum lipid profile in the form of total cholesterol (TC), high-density lipoprotein-cholesterol (HDLC), low-density lipoprotein-cholesterol (LDLC), very low-density lipoprotein-cholesterol (VLDLC) and triglycerides (TGL) was analyzed on the same day of the withdrawal of blood.

The serum cholesterol was estimated by taking 10 μL of distilled water, 10 μL of sample and 10 μL of cholesterol standard in three separate test tubes. One thousand microliters of cholesterol reagent was added to all three test tubes. The mixtures were incubated at 37°C for 10 min and the absorbance of standard and sample was measured against the blank at 505 nm in the analyzer.

The serum TGL was estimated by taking 10 μL of distilled water, 10 μL of sample and 10 μL of TGL standard in three separate test tubes. One thousand microliters of TGL reagent was added to all three test tubes. The mixtures were incubated at 37°C for 10 min and the absorbance of standard and sample was measured against the blank at 505 nm in the analyzer.

Serum HDLC was estimated by mixing 250 μL of serum sample with 500 μL of HDL precipitating reagent, followed by 10 min incubation at room temperature. The mixture was centrifuged at 4000 rpm for 10 min to obtain a clear supernatant. Fifty microliters of distilled water, 50 μL of supernatant and 50 μL of HDLC standard were taken in three separate test tubes. One thousand microliters of cholesterol reagent was added to all three test tubes. The mixtures were incubated at 37°C for 10 min and the absorbance of the standard and sample was measured against the blank at 505 nm in the analyzer.

LDLC and VLDLC levels were calculated as shown below:

LDLC = Total cholesterol – (VLDLC) – (HDLC)

VLDLC = Triglycerides/5

Statistical analysis

Evaluation of results and statistical analysis was carried out using Student's *t*-test. The comparison between well-differentiated, moderately differentiated and poorly differentiated carcinoma groups was done using one-way Analysis of Variance. In all the above tests, *P* value < 0.05 was taken to be statistically significant; *P* value > 0.05 was taken to be statistically not significant.

RESULTS

Among 75 subjects included in the present study, 40 (53%) were males and 35 (47%) were females, with an age range of 30-75 years and mean age of 51.07 years. The oral cancer and control groups were subdivided into two subgroups: Subjects WHT and subjects NHT.

Serum lipid profile in oral cancer and control group

The mean serum lipid profile values of oral cancer and control groups are represented in Table 1. The *P* values were <0.01, suggesting that, statistically, there was a highly significant reduction of mean serum TC, HDLC and TGL in the subjects of oral cancer as compared with the control group. The mean serum values of LDLC and VLDLC were reduced in the oral cancer group as compared with the control group, but this reduction was not statistically significant.

The intergroup evaluation of serum lipid profile levels in well-differentiated, moderately differentiated and poorly differentiated carcinoma in the oral cancer group did not show a significant correlation of serum TC, HDLC, LDLC, VLDLC and TGL between the degrees of differentiation. The distribution of mean serum lipid profile levels in oral cancer subjects according to their degree of differentiation is as depicted in Table 2.

Serum lipid status in the no habit of tobacco and with habit of tobacco groups

Of the 75 subjects included in this study, 48 subjects were having a habit of tobacco and the remaining 27 subjects were not having any habit of tobacco. The mean serum lipid profile between NHT and WHT subjects of each group (oral cancer and control) was compared. When the mean serum TC, HDLC, LDLC, VLDLC and TGL levels

Table 1: Comparison of serum lipid profile levels in oral cancer and control groups

Parameters assessed	Control (*N*=25) Mean±SD	Oral cancer (*N*=50) Mean±SD	*P* value*
TC	193.76±8.64	178.56±14.66	<0.001
TGL	112.36±11.75	100.78±12.39	<0.001
HDLC	48.40±6.53	40.78±7.13	<0.001
LDLC	121.48±23.73	117.02±21.34	0.41
VLDLC	24.56±8.50	23.30±6.10	0.46

N: Number of subjects, TC: Total cholesterol, TGL: Triglycerides, HDLC: High-density lipoprotein-cholesterol, LDLC: Low-density lipoprotein-cholesterol, VLDLC: Very low-density lipoprotein-cholesterol; **P* value <0.05-statistically significant; *P* value>0.05-statistically not significant

between oral cancer NHT and WHT and control NHT and WHT subjects were compared, there was no statistically significant difference between them [Table 3].

The serum lipid levels of WHT subjects in oral cancer were compared with the serum lipid profile levels of WHT subjects in the control group to eliminate any bias because of tobacco habit. The mean serum TC, HDLC and TGL levels showed statistically significant reduction in the oral cancer group as compared with the control group, whereas LDLC and VLDLC did not show a statistically significant reduction [Table 3].

DISCUSSION

Cholesterol and TGL are important lipid constituents of the cell and are essential to carry out several vital physiological functions. Cholesterol is essential for maintenance of the structural and functional integrity of all biological membranes. It is also involved in the activity of membrane-bound enzymes and is important for stabilization of the DNA helix. Cellular uptake and regulation of cholesterol is mediated by lipoprotein receptors especially located on the surface of the cells. For transport in plasma, TGL and cholesterol are packaged into lipoproteins, which are then taken up and degraded by cells to fulfill the demands for cellular functions.[5]

Table 2: Serum lipid profile in the oral cancer group according to their histological grade

Parameters assessed	Well differentiated (*N*=14) Mean±SD	Moderately differentiated (*N*=27) Mean±SD	Poorly differentiated (*N*=9) Mean±SD
TC	175.64±14.78	179.93±14.91	179.00±14.75
TGL	102.50±11.23	101.96±13.20	94.56±10.71
HDLC	40.43±7.05	41.63±7.54	38.78±6.22
LDLC	127.21±20.31	113.37±20.19	112.11±23.23
VLDLC	23.86±6.49	23.41±5.67	22.11±7.27

N: Number of subjects, TC: Total cholesterol, TGL: Triglycerides, HDLC: High-density lipoprotein-cholesterol, LDLC: Low-density lipoprotein-cholesterol, VLDLC: Very low-density lipoprotein-cholesterol

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 question arises whether hypolipidemia is a predisposing factor or result of cancer. 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.[5,9,10-14]

Cholesterol is an essential constituent of lipoprotein fractions like HDLC, LDLC and VLDLC. Seventy-five percent of the plasma cholesterol is transported in the form of LDLC. Body cells sequester cholesterol from the LDLC fraction of lipoproteins. LDL receptors are necessary for metabolizing circulating LDLC levels and nearly 80% of the plasma LDLC is cleared by LDL receptors.[5,7,15] High activity of LDL receptors attributes for lowering the serum cholesterol levels.[5,7,16] In the present study, a highly significant reduction was observed in the levels of TC in the oral cancer group as compared with the controls thus supporting the hypothesis postulated above. Several prospective and retrospective studies have shown an inverse association between blood lipid profile and different cancers.[2,4,5,7,17-19] Lohe *et al.* have observed an inverse relationship between serum lipid profile and oral cancer and oral precancer.[6] Patel *et al.* have also observed an inverse relationship between lower plasma lipid profile and head and neck malignancies and oral precancerous conditions.[5,7] Furthermore, some investigators have also found a relation of low serum cholesterol with increased risk of cancer occurrence and mortality.[5,6,9,20-22]

HDLC levels may be a useful indicator, reflecting the initial changes occurring in neoplastic conditions.[7] A drastic reduction in levels of HDLC was observed in our study, which is in accordance with previous reports[2,5,6,19,23,24] stating that low HDLC 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.[5,23]

Table 3: Serum lipid profile comparison between no habit of tobacco and with habit of tobacco subjects in the oral cancer and control groups

Parameters assessed	Control (*N*=25)		Cancer (*N*=50)		*P* value comparison*		
	NHT (*N*=15) Mean±SD	WHT (*N*=10) Mean±SD	NHT (*N*=12) Mean±SD	WHT (*N*=38) Mean±SD	Control NHT with control WHT	Cancer NHT with cancer WHT	Control WHT with cancer WHT
TC	192.40±8.85	195.80±8.32	181.00±15.20	177.79±14.61	0.34	0.51	<0.001
TGL	111.80±12.13	113.20±11.75	105.33±12.02	99.34±12.31	0.77	0.14	0.001
HDLC	48.47±6.44	48.30±7.02	40.92±7.80	40.74±7.01	0.95	0.94	0.004
LDLC	116.87±21.08	128.40±26.87	120.67±13.11	115.87±23.37	0.24	0.50	0.16
VLDLC	24.87±9.36	24.10±7.48	24.83±6.10	22.82±6.10	0.83	0.32	0.61

N: Number of subjects, NHT: Subjects with no habit of tobacco, WHT: Subjects with habit of tobacco, TC: Total cholesterol, TGL: Triglycerides, HDLC: High-density lipoprotein-cholesterol, LDLC: Low-density lipoprotein-cholesterol, VLDLC: Very low-density lipoprotein-cholesterol **P* value <0.05-statistically significant; *P* value> 0.05-statistically not significant

We observed significantly decreased TGL levels in cancer patients as compared with the controls, which is in agreement with the previous studies.[5,23] However, Alexopoulos *et al.* have found a non-significant difference in serum TGL between controls and patients,[5,18] while others have observed elevated TGL levels in cancer patients.[2,5,25] Serum LDLC and VLDLC levels did not reveal any significant difference between the two groups. Similar results for LDLC and VLDLC were observed in a study conducted by Chawda *et al.*[23]

Histopathologically, the oral cancer group was graded as well-differentiated, moderately differentiated or poorly differentiated squamous cell carcinoma. While comparing all the lipid levels between the three different groups of oral cancer patients, there was no statistically significant difference found. The results of our study were in accordance with the studies conducted by Lohe *et al.* and Chawda *et al.*[6,23]

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.[5,6,26]

In the present study, the majority of the subjects in the oral cancer group were having a habit of tobacco consumption. When the mean serum TC, HDLC, LDLC, VLDLC and TGL levels between oral cancer NHT and WHT and control NHT and WHT subjects were compared, there was no statistically significant difference in their levels. But, when the serum lipid levels of WHT subjects in the oral cancer group were compared with the serum lipid profile levels of the WHT control group to eliminate any bias because of tobacco habit, significant lower levels of mean serum TC, HDLC and TGL were found in the WHT group of oral cancer as compared with the WHT group of control subjects. Mean serum LDLC and VLDLC levels did not reveal any significant difference among the two groups. These findings imply that lower lipid levels may be mainly because of the basic underlying disease process and not because of tobacco habit. This suggests that although the role of tobacco has been established as an etiological factor for oral cancer, it may not have a direct and overall significant association with serum lipid levels.

CONCLUSION

The results of the present study show evidence of an inverse relationship between the serum lipid profile values of TC, HDLC, TGL and oral cancer. The mean serum lipid profile levels between histological grading of the oral cancer had no statistical significance. The findings of this study suggest that serum lipid profile may be used as a biochemical indicator but has no direct and overall significant influence associated with tobacco habit. The lower serum lipid status may be considered a useful 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 cancer. Hence, the present findings strongly warrant an in-depth study of alterations in serum lipid profile patterns in patients with oral cancer.

REFERENCES

1. Schatzkin A, Hoover RN, Taylor PR, Ziegler RG, Carter CL, Albanes D, *et al*. Site-specific analysis of total serum cholesterol and incident cancers in the National Health and Nutrition Examination Survey I epidemiologic follow-up study. Cancer Res 1988;48:452-8.
2. Halton JM, Nazir DJ, McQueen MJ, Barr RD. Blood lipid profiles in children with acute lymphoblastic leukemia. Cancer 1998;83:379-84.
3. Simo CE, Orti LA, Sena FF, Contreras BE. Blood cholesterol in patients with cancer. An Med Interna 1998;15:363-6.
4. Allampallam K, Dutt D, Nair C, Shetty V, Mundle S, Lisak L, *et al*. The clinical and biologic significance of abnormal lipid profiles in patients with myelodysplastic syndromes. J Hematother Stem Cell Res 2000;9:247-55.
5. Patel PS, Shah MH, Jha FP, Raval GN, Rawal RM, Patel MM, *et al*. Alterations in plasma lipid profile patterns in head and neck cancer and oral precancerous conditions. Indian J Cancer 2004;41:25-31.
6. Lohe VK, Degwekar SS, Bhowate RR, Kadu RP, Dangore SB. Evaluation of correlation of serum lipid profile in patients with oral cancer and precancer and its association with tobacco abuse. J Oral Pathol Med 2010;39:141-8.
7. Gupta S, Gupta S. Alterations in serum lipid profile patterns in oral cancer and oral precancerous lesions and conditions—a clinical study. Indian Journal of Dentistry 2011;2:1-7.
8. Chyou PH, Nomura AM, Stemmermann GN, Kato I. Prospective study of serum cholesterol and site-specific cancers. J Clin Epidemiol 1992;45:287-92.
9. Eichholzer M, Stahelin HB, Gutzwiller F, Ludin E, Bernasconi F. Association of low plasma cholesterol with mortality for cancer at various sites in men: 17-y follow-up of the prospective basel study. Am J Clin Nutr 2000;71:569-74.
10. Feinleib M. Review of epidemiological evidence for a possible relationship between hypocholesterolemia and cancer. Cancer Res 1983;43:2503s-7s.
11. Dyer AR, Stamler J, Paul D, Shekelle RB, Schoenberger JA, Berkson DM, *et al*. Serum cholesterol and risk of death from cancer and other causes in three Chicago epidemiological studies. J Chronic Dis 1981;34:249-60.
12. Kark JD, Smith AH, Switzere BR, Hames CG. Retinol, carotene, and the cancer/cholesterol association. Lancet 1981;1:1371-2.
13. Kark JD, Smith AH, Hames CG. Serum retinol and the inverse relationship between serum cholesterol and cancer. Br Med J 1982;284:152-4.
14. Peto R, Doll R, Buckley JD, Sporn MB. Can dietary beta-carotene materially reduce human cancer rates? Nature 1981;290:201-8.
15. Kesaniemi YA, Witzlum JL, Heinbrecher UP. Receptor-mediated catabolism of low density lipoprotein in man. Quantitation using glycosylated lipoprotein. J Clin Invest 1983;71:950-9.
16. Brown MS, Kovanen PT, Goldstein JL. Regulation of plasma

cholesterol by lipoprotein receptors. Science 1981;212:628-35.
17. Gilbert MS, Ginsberg H, Fagerstrom R, Brown WV. Characterization of hypocholesterolemia in myeloproliferative disease: Relation to disease manifestations and activity. Am J Med 1981;71:595-602.
18. Alexopoulos CG, Blatsios B, Avgerinos A. Serum lipids and lipoprotein disorders in cancer patients. Cancer 1987;60:3065-70.
19. Budd D, Ginsberg H. Hypocholesterolemia in acute myelogenous leukemia. Association between disease activity and plasma low density lipoprotein cholesterol concentrations. Cancer 1986;58:1361-5.
20. Larking PW. Cancer and low levels of plasma cholesterol: The relevance of cholesterol precursors and products to incidence of cancer. Prev Med 1999;29:383-90.
21. Williams RR, Sorlie PD, Feinleib M, McNamara PM, Kannel WB, Dawber TR. Cancer incidence by levels of cholesterol. J Am Med Assoc 1981;245:247-52.
22. Cambein F, Ducimetiere P, Richard J. Total serum cholesterol and cancer mortality in a middle-aged male population. Am J Epidemiol 1980;112:388-94.
23. Chawda JG, Jain SS, Patel HR, Chaduvula N, Patel K. The relationship between serum lipid levels and the risk of oral cancer. Indian J Med Paediatr Oncol 2011;32:32-5.
24. Dessi S, Batetta B, Pulisci D, Spano O, Cherchi R, Lanfranco L, *et al*. Altered pattern of lipid metabolism in patients with lung cancer. Oncology 1992;49:436-41.
25. Favrot MC, Dellamonica C, Souillet G. Study of blood lipids in 30 children with a malignant hematological disease or carcinoma. Biomed Pharmacother 1984;38:55-9.
26. Ames BN. Dietary carcinogens and anticarcinogens: Oxygen radicals and degenerative diseases. Science 1983;221:1256-64.

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