



EVALUATION OF SERUM LIPID PROFILE IN ORAL CANCER, POTENTIALLY MALIGNANT DISORDERS AND IN PATIENTS WITH TOBACCO HABIT—A CASE CONTROL STUDY.

Dental Science

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ABSTRACT

Lipids are major cell membrane components essential for various biological functions including cell growth and division of normal and malignant tissues. This study aim in evaluating serum lipid profile in patients with oral cancer(OC), potentially malignant disorders(PMDs), and patients with tobacco habit.

Methodology: This study consist of 4 groups ie OC, PMDs, patients with habit of tobacco & Control group. 10 ml of fasting venous blood from all the subjects. Serum from this collected blood sample is used for the evaluation using BS-380 chemist autoanalyser and the results are subjected to statistical analysis using SPSS 16 software. The test applied is one way ANOVA.

Result: Serum TC is substantially reduced in OC, PMDs ($P<0.001$), ($P<0.05$) respectively. There is no significant change of TC in patients with habit ($P>0.05$). Serum TG is substantially reduced in OC patients when compared with PMDs, habit and control & is statistically significant ($P<0.001$). There is no significant change of TG in patients with PMDs, habit and control ($P>0.05$). Serum HDL is substantially reduced in OC & PMDs which is statistically highly significant ($P<0.001$). Patients with habit also showed lowered levels of HDL when compared with control but not statistically significant ($P>0.05$). There is decreased HDL in habit patient also but not significantly. The mean serum levels of LDL in all the groups ($P>0.001$) found that there is no significant changes. VLDL is substantially reduced in oral cancer patients which is statistically significant ($P<0.001$). There is no significant change of VLDL in patients in PMDs and habit patients ($P>0.05$).

Conclusion: There is inverse relation between serum lipid profile and occurrence of OC & PMDs with no direct and overall significant influence associated with tobacco habit.

KEYWORDS

Oral cancer, potential malignant disorders, lipid profile, tobacco habit.

INTRODUCTION

Oral cancer is one of the most prevalent cancers and is one of the 10 most common causes of death. Oral cancer(OC) develop from potentially malignant disorders (PMDs). Habit of tobacco consumption and alcohol is a known etiological factor for development of oral cancer. Various biochemical evaluation have shown that various substances alter quantitatively in the serum during tumor development and are referred as tumor markers.¹ These are diagnostic and prognostic biomarkers which are quantifiable traits that help clinical oncologists at the first interaction with the suspected patients. These particularly aid in, identifying who is at risk, early diagnosis prompt treatment and prognosis of the disease.² So, if the biochemical changes occur even before frank cancer has occurred, one can predict whether a particular individual with the underlying biochemical defect would develop OC or not at a later date from existing precancerous state.

Lipids are major cell membrane components essential for various biological functions including cell growth and division of normal and malignant tissues. The major lipids in the bloodstream are cholesterol and triglycerides which are insoluble in the blood. The large particles of cholesterol, triglycerides and proteins are the lipoproteins. As part of lipoproteins the cholesterol and triglycerides can be carried around in the blood stream. The major lipoproteins are low density lipoproteins (LDL), very low density lipoproteins (VLDL), and high density lipoproteins (HDL) which gets altered.

Hence this case control study aim in evaluating serum lipid profile in patients with OC, PMDs, and patients with tobacco habit.

Methodology: This is a case control study having 4 groups; of whom 20 patients are with OC, 20 patients are with oral PMDs, and 20 patients with habit of tobacco& 20 healthy. All groups consisted of both sexes and are in the age group of 15 years to 60 years. Patients who have any medical problems like cardiac disease, diabetes, renal disease etc are excluded from the study. Biopsy was taken from such of the patients who are clinically confirmed to have OC or PMDs. Fasting venous blood from patients and control group of about 10ml is collected in a test tube and the serum is separated from other constituents of blood using centrifuge. Serum from this collected

blood sample is used for the evaluation. The biochemical evaluation is done using BS-380 chemist autoanalyser and the results are analyzed and expressed. Estimation of Serum Lipid profile includes Total Cholesterol (TC), Triglycerides (TG), High density lipids (HDL), Low density lipids(LDL) and Very low density lipids (VLDL). The method for estimation of lipids is Peroxidase method (POD). The values of the test are analyzed and subjected to statistical evaluation. TC, TG, HDL, LDL, VLDL are compared in OC, PMDs, tobacco habit patients and controls.

RESULTS: The mean serum levels of total cholesterol (TC), triglycerides, high density lipoproteins, low density lipoproteins, and very low density lipoproteins are compared with the control, patients with OC, PMDs and patients with habit of tobacco chewing and represented in Graph- I, Graph- II, Graph- III, Graph- IV, Graph- V. Comparison of the level of serum TC, triglycerides, high density lipoproteins, low density lipoproteins, and very low density lipoproteins among the four groups is done by one way ANOVA and represented in Table I, Table II, Table III, Table IV, Table V respectively. It is found that mean value between groups is statistically significant and hence there is significant decrease of TC. ($P<0.001$) (Table- I). Serum TC is substantially reduced in OC patients which is statistically significant ($P<0.001$). Oral PMDs also showed lowered levels of TC when compared to patients with habit and control ($P<0.05$). There is no significant change of TC in patients with habit ($P>0.05$). The value suggests that there is significant decrease of TC in OC patients and PMDs. There is decrease in TC patients with habit not statistically significant. Serum TG is substantially reduced in OC patients when compared with PMDs, habit and control which is statistically significant ($P<0.001$). There is no significant change of TG in patients with PMDs, habit and control ($P>0.05$). Suggesting that there is significant decrease of TG in OC patients but there is no change of TG in PMDs and patients with habit (Table-II). Serum HDL is substantially reduced in OC patients and oral PMDs which is statistically highly significant ($P<0.001$). Patients with habit also showed lowered levels of HDL when compared with control but not statistically significant ($P>0.05$). Suggesting that there is significant decrease of HDL in OC patients and PMDs, with decreased HDL in habit patient also but not significantly. (Table -III). The mean serum levels of LDL are compared with the control, patients with OC, PMDs

and patients with tobacco habits. It was ($P>0.001$) found that there is no significant changes. (Table -IV) VLDL is substantially reduced in oral cancer patients which is statistically significant ($p<0.001$). There is no significant change of VLDL in patients in PMDs and habit patients ($P>0.05$). Suggesting that there is significant decrease of VLDL in oral cancer patients but not in PMDs and habit patients (Table- V).

Graph- I Bar graph showing comparison of four groups with respect to total cholesterol

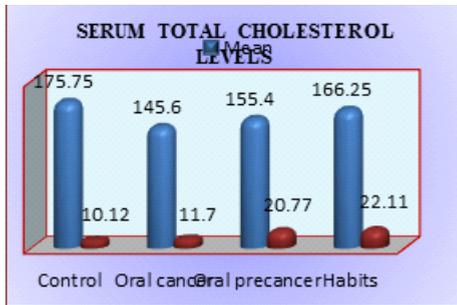


Table- I Comparison of four groups with respect to total cholesterol by one way Anova

Source of variation	Degrees of freedom	Sum of squares	Mean sum of squares	P-value
Between groups	3	10267.9	3422.633	0.001***
Within groups	76	22037.10	289.96	
Total	79	32305.00		

*** $p<0.001$

Graph- II Bar graph showing comparison of four groups with respect to triglyceride

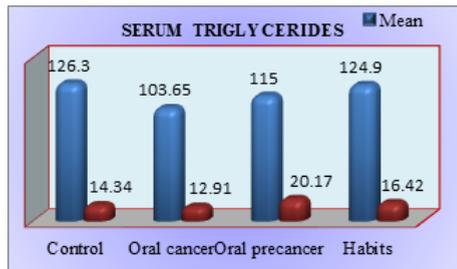


Table -II: Comparison of four groups with respect to triglycerides by one way Anova

Source of variation	Degrees of freedom	Sum of squares	Mean sum of squares	P-value
Between groups	3	6605.33	2201.77	0.001***
Within groups	76	19940.55	262.37	
Total	79	26545.88		

*** $p<0.001$

Graph-III Bar graph showing comparison of four groups with respect to high density lipids

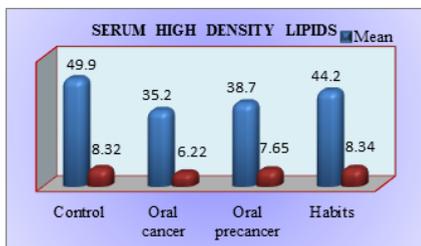


Table- III Comparison of four groups with respect to high density lipids by one way anova

Source of variation	Degrees of freedom	Sum of squares	Mean sum of squares	P-value
Between groups	3	6605.33	2201.77	0.001***
Within groups	76	19940.55	262.37	
Total	79	26545.88		

Source of variation	Degrees of freedom	Sum of squares	Mean sum of squares	P-value
Between groups	3	2487.60	829.200	0.001***
Within groups	76	4482.40	58.97	
Total	79	6970.00		

*** $p<0.001$

Graph -IV Bar graph showing comparison of four groups with respect to low density lipids

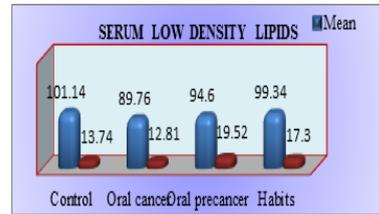


Table -IV Comparison of four groups with respect to low density lipids by one way Anova

Source of variation	Degrees of freedom	Sum of squares	Mean sum of squares	P-value
Between groups	3	1564.94	521.64	0.11
Within groups	76	19638.98	258.40	
Total	79	21203.92		

$p>0.05$

Graph -V Bar graph showing comparison of four groups with respect to very low density lipids

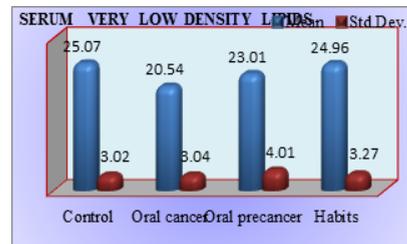


Table-V Comparison of four groups with respect to very low density lipids by one way anova

Source of variation	Degrees of freedom	Sum of squares	Mean sum of squares	P-value
Between groups	3	271.08	90.36	0.001***
Within groups	76	859.55	11.31	
Total	79	1130		

*** $p<0.001$

DISCUSSION: The result and observation of serum lipid profile assay in this study shows that there are substantial lower levels of TC and HDL in OC patients and PMDs as compared with control ($P<0.001$) with decrease of TC in habit patients also but not significantly ($P>0.05$), but HDL levels showed decrease in habit patients, but not significant ($P>0.05$). TG and VLDL were significantly decreased in OC ($P<0.001$) but not in PMDs or habit patients ($P>0.05$). However LDL did not reveal any significant difference in any group. The results of this study coincides with Patel H. R. et al. their result showed significantly decreased TC, HDL, VLDL and TG levels in OC patients as compared to the controls which is consistent with our findings. They also found significant decreased TC, HDL, TG and VLDL in PMDs patients also, 3 but in the present study there is no significant decrease of TG and VLDL in PMDs. However LDL levels showed no significant decrease in their study which is similar to the present study.

Studies by Hoyer AP 4 found that there is significant decrease of HDL and with no significant change in LDL levels in breast cancer as compared to control which is similar to our finding but, in their study they found no association of TC in breast cancer, in present study TC is also inversely associated. Chou PH et al. 5 also found inverse trend of lipid profile in oral, pharyngeal, oesophagus, with significant decrease of TC in cancer of colon, which is similar to our findings.

According to K. Allapallam et al.⁶ TC and HDL are decreased in patients with myelodysplastic syndrome when compared with control which is similar to our findings, but they also found decreased LDL levels in their studies, but in this study there is no change in LDL levels. They substantiated their findings mentioning that there is excessive intracellular lipid biosynthesis in the expanding clone.

There are the 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 the cancer, but the association with cancer is secondary which indicates that cholesterol serves as a marker for some other causal variable or 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.⁷

Williams et al. mentioned that one of the postulated mechanisms for the lower level of serum cholesterol in cancer patients is that there is increased membrane permeability to carcinogens induced by transfatty acids.⁸

However, few studies have reported that hypolipidemia may result because of the direct lipid lowering effect of tumor cells or some secondary malfunction of the lipid metabolism or secondary to antioxidant vitamins.

It is widely demonstrated that oral cancer interferes significantly on food intake as well as on lipid ingestion and absorption. Therefore, it can be expected that subjects with oral cancer have low serum levels of lipids, but the other factors, such as genes and hormones, also interact to regulate the plasma cholesterol levels in man.

Because of the continuous cycling of cholesterol into and out of the blood stream, the plasma cholesterol concentration is not a simple additive function of dietary cholesterol intake and endogenous cholesterol synthesis. Rather, it reflects the rate of synthesis of the cholesterol carrying lipoproteins and the efficiency of the receptor mechanisms that determine their catabolism. Thus, the cholesterol homeostasis in healthy subjects depends on the presence and function of specific receptors on the cell surface. These receptors normally control the degradation of LDL, the major cholesterol transport protein in human plasma. In the neoplastic disease, an increased LDL activity in tumor cell may produce hypocholesterolemia.⁹

Low levels of lipids could be due to the process of carcinogenesis, ⁹ because of lipid peroxidation there is greater utilization of these lipids for new membrane biogenesis. Seventy five percent of the plasma cholesterol is transported in the form of LDL. Body cells sequester cholesterol from LDL fraction of lipoproteins. LDL receptors are necessary for metabolizing circulating LDL levels and nearly 80% of the plasma LDL is cleared by LDL receptors.¹⁰

High activity of LDL receptors attributes for lowering the serum cholesterol levels. The individuals having deficient or defective LDL receptors remove plasma LDL at much lower rate and have considerably elevated levels.

High density lipoprotein (HDL) levels may be a useful indicator reflecting initial changes occurring in PMDs. A significant decrease in levels of HDL was also observed in present study. This was in accordance with previous reports which reported that lower HDL is an additional predictor of oral PMDs and it might be a consequence of disease that is mediated by utilization of cholesterol by membrane biogenesis.¹⁰

VLDL contains highest amount of triglycerides. Any change in triglyceride levels will also change VLDL levels. VLDL is converted to LDL after transporting triglycerides to their target cells. However the role of triglycerides in explaining the overall pattern of total cholesterol change is less clear.¹¹

Some of the previous studies stated that serum cholesterol levels were

inversely associated with incidence of cancer.^{12, 13}, Dianzani reviewed the problem of the pattern of lipid peroxidation in cancer cells.¹⁴

They found that during carcinogenesis, the loss of lipid peroxidation is already evident at the stage of preneoplastic nodules. Our study performed on PMDs also showed inverse relation between serum cholesterol levels and PMDs, these changed levels might indicate the progression of these lesions towards malignancy.

In this study mean serum TC, TG, LDL, VLDL, did not show significant changes in habit patients without any lesion except for marginal decreased HDL levels. These finding imply that the lower lipid levels may be because of basic underlying disease process and not because of only tobacco habit. The decrease in mean serum HDL level observed in tobacco habituates of this study may be attributed to tobacco habituates in whom the good cholesterol (HDL) level is provenly reduced. This suggests that although the role of tobacco has been established in the etiology of OC and PMDs, it may not have direct and overall significant association with serum lipid profile.

Furthermore, some investigators have also found relation of low serum cholesterol with increased risk of cancer occurrence and mortality.^{3, 12} Rose and Shipley reported 66% higher mortality rate because of cancer in the group of cancer patients with the lowest plasma cholesterol than in the highest plasma cholesterol.¹³

The results of 5 parameters (TC, TG, HDL, LDL, and VLDL) of lipid profile tested in this study are in agreement with above mentioned studies done in cancers at various sites of body. However there are differences between the studies when various parameters are considered individually which might be due to various reasons such age of the patients, methodology etc.

CONCLUSION: The following conclusions can be drawn from this study, the Serum lipid profile show significant correlation with OC and PMDs independently. There is inverse relation between serum lipid profile and occurrence of OC & PMDs. That serum lipid profile, as a biochemical indicator, has got no direct and overall significant influence associated with tobacco habit.

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