Serum Lipid Profile In Patients With Oral Tobacco Habits and Oral Precancer Lesions and Conditions

Corresponding Author:
Dr. Stuti Goyal,
Senior Lecturer, Sri Sai College of Dental Surgery, Oral Medicine and Radiology - India

Submitting Author:
Dr. Stuti Goyal,
Senior Lecturer, Sri Sai College of Dental Surgery, Oral Medicine and Radiology - India

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Author(s): Goyal S, C V, K S, Ch L

Abstract

Background & Objectives: Tobacco carcinogens induce generation of free radicals and reactive oxygen species, which cause lipid peroxidation. Because of the lipid peroxidation, there is a greater utilization of lipids for new membrane biogenesis. Hence the present study was carried out to determine the variations, if any, in the serum lipid profile of subjects with tobacco habit and patients with oral precancers.

Methodology: The study consisted of 30 healthy controls, 30 patients with oral tobacco habit and 30 oral precancer cases. After thorough clinical oral screening for all the subjects of the groups and histopathological confirmation for premalignancy, 5 ml of fasting blood was collected. Blood was allowed to clot and serum separated. The serum triglycerides were estimated by the GPO-PAP, End Point Assay method; Total cholesterol by CHOD-PAP and HDL-Cholesterol by PEG-CHOD-PAP, End Point Assay method with Lipid Clearing Factor (LCF). The LDL and VLDL levels were calculated using the Friedewald’s equation. One way ANOVA SPSS version 19.0 was used for statistical analysis.

Results: In the present study there was no statistically significant change in values of serum lipid profile in either the oral tobacco habit group or the oral precancer group when compared with age and sex matched controls. There was no statistical significant change in the lipid profile parameters on comparing oral tobacco habit group with oral precancer group also.

Conclusion: Therefore it was concluded that oral precancer, though it represents 'potentially malignant lesions', it is localized and hence might not cause a significant serum lipid profile change as frank cancers do. Hence the precancorous lesions might not have the required need for greater utilization of lipids for new membrane biogenesis, which are fulfilled by synthesis or degradation of the circulating lipids in the blood, which might cause a significant change in the serum lipid profile values.

Introduction

Lipids are major cell membrane components, essential for various biological functions including cell growth and division of normal and malignant tissues. Tobacco carcinogens induce generation of free radicals and reactive oxygen species, which cause lipid peroxidation. Because of the lipid peroxidation, there is a greater utilization of lipids for new membrane biogenesis. Cells fulfill these requirements either from circulation, by synthesis through the metabolism or from degradation of major lipoprotein fractions like VLDL, LDL or HDL. Usage of only tobacco/ tobacco with other ingredients (areca nut) is responsible for...
causing various oral precancers. Premalignancy / precancer can be defined as any lesion that displays the metabolic and histologic activity found in cancerous lesions and within whose boundaries it is possible, but not mandatory, for a carcinoma to develop. Oral cancer lesions are usually preceded by the occurrences of premalignant lesions and / or conditions. Malignant transformation of Oral Leukoplakia, a premalignant lesion is 1% to 2% over 5 years, while Oral Lichen planus (OLP) and Oral Sub Mucous Fibrosis (OSMF), both being premalignant conditions have malignant transformation of 0.05% in 10 years and 5% to 8% respectively. Researchers have reported association of plasma/serum lipids and lipoproteins with different cancers, as cholesterol is essential for maintenance of structural & functional integrity of all biological membranes. As neoplastic disease is related to new growth, there is a greater utilization of lipids including total cholesterol, lipoproteins and triglycerides for new membrane biogenesis. Cells fulfill these requirements either from circulation, by synthesis through the metabolism or from degradation of major lipoprotein fractions like VLDL, LDL or HDL.

The idea of screening and following patients by blood test is appealing from several points of view, which include, it’s ease, economic advantage, non-invasiveness and possibility of repeated sampling. Hence the present study has been taken up to evaluate the variation in serum lipid profile (total cholesterol(TC), VLDL, LDL, HDL & total TG levels) if any, in patients with oral tobacco habits and in oral precancer lesions and conditions.

Materials And Methods

The study was conducted in the Department of Oral Medicine and Radiology, Sri Sai College of Dental Surgery, Vikarabad. A total sample size of 90 subjects was chosen, with study group consisting of a total of 30 patients each in Precancer group and Tobacco Habit group. The control group consisted of 30 age and sex matched individuals, without any systemic or oral condition. The controls and patients selected belonged to similar socio-economic background. Any subject with systemic disease (eg: diabetes mellitus, thyroid disorders and liver dysfunction) and taking any drugs (including steroids) for the same were excluded. Obese subjects weighing more than 20% above the ideal weight were excluded. The tobacco habit group subjects were selected on the basis of the study by Robson N. et al., who have defined a current smoker as someone who had smoked > 100 cigarettes in their lifetime and who at the time of the study reported that they were smoking. (U.S. Department of Health and Human Services 1996) and a current smokeless tobacco chewer as defined by Ernster VL. et al., (1990) in their study, as one who has used smokeless tobacco more frequently than once a month and who had used smokeless tobacco within the previous month.

After obtaining informed consent, patients were tested for fasting blood glucose levels, and complete blood picture to rule out diabetes mellitus. An incisional biopsy was performed, if clinical evidence of oral precancer lesion and/or condition was present. After the confirmation of the precancerous state, 5 ml of fasting (12-14hrs) blood sample was collected in a sterile bottle and allowed to clot for about an hour at 37°C. The serum was then separated and stored at 4°C. The serum triglycerides were estimated by the GPO-PAP (Glycerol-3-phosphate Oxidase – Peoxidase), End Point Assay; Total cholesterol by CHOD-PAP (Cholesterol Oxidase – Peroxidase) and HDL-Cholesterol by PEG-CHOD-PAP(Polyethylene glycol 6000- Cholesterol Oxidase – Peroxidase), End Point Assay with Lipid Clearing Factor (LCF). The LDL Cholesterol level was calculated by the Friedewald’s equation.

\[ \text{VLDL= triglycerides/5} \]  
\[ \text{LDL=Total Cholesterol- HDL-VLDL.} \]

The data collected was tabulated based upon the LDL, VLDL, HDL, total cholesterol and serum triglyceride levels separately for each of the three groups and subjected to statistical analysis. One way ANOVA SPSS version 19.0 was used for multiple group comparison for statistical analysis. For all the tests p value of 0.05 or less was used for statistical significance.

Results

Each group comprised of 26 males (86.7 %) and 04 (13.3 %) females (Graph 1). The age range for all the three groups ranged from 19 – 70 years. The mean age and standard deviation (SD) of Control group was 30.80±12.11, Tobacco habit group was 31.07±11.87 and that of Precancer group was 30.83±12.21 (Graph 2). Comparison between age and various serum lipid profile parameters done, and it was found that there is no association between age and any of the serum lipids.

The Tobacco Habit study group consisted of 11 subjects (07 males; 04 females) with tobacco chewing
habit (46.7%), 14 subjects (all males) with tobacco smoking habit (36.7%) and 05 subjects (all males) with tobacco chewing and smoking (16.7%). The Precancer study group consisted of 17 subjects (15 males; 02 females) with OSMF, 09 subjects (07 males; 02 females) with OLP and 04 subjects (all males) with Oral Leukoplakia. Therefore the patients with OSMF formed a majority representing 56.6 % of the group, while the patients of OLP represented 30 %, and the patients with Oral Leukoplakia represented the least of the group at 13.4 %.

The control group lipid profile parameters were - TG with mean and SD of 118.73±31.45 and ranging between 50 mg/dl to 210 mg/dl, TC with mean and SD of 179.70 ± 15.64 and ranging from 148 mg/dl to 236 mg/dl, LDL Cholesterol with mean and SD of 106.57 ± 15.97 and ranging from 78 mg/dl to 166 mg/dl, HDL Cholesterol with mean and SD of 49.27 ± 4.28 and ranging from 44 mg/dl to 62 mg/dl and the VLDL Cholesterol with mean and SD of 23.73 ± 6.27 and ranging from 10 to 42 mg/dl.

The Tobacco Habit group lipid profile parameters were- TG with mean and SD of 123.30 ±70.90 and ranging between 56 mg/dl to 464 mg/dl, TC with mean and SD of 186.20 ± 29.60 and ranging from 142 mg/dl to 312 mg/dl, LDL Cholesterol with mean and SD of 115.70 ± 28.56 and ranging from 81 mg/dl to 245 mg/dl, HDL Cholesterol with mean and SD of 45.90 ± 5.66 and ranging from 34 mg/dl to 56 mg/dl and the VLDL Cholesterol with mean and SD of 24.60 ± 14.22 and ranging from 11 to 93 mg/dl.

The serum lipid profiles of the habit group are within normal range except for few patients. Triglycerides levels were above normal level (<165 mg/dl) for two subjects while tobacco level was above normal level (<239 mg/dl) for only one subject. LDL levels were normal (<180 mg/dl) for all the subjects except one, in whom it was raised. HDL levels were below normal (>40 mg/dl) for only four subjects while VLDL level (<40 mg/dl) was raised for only one subject. In the control group, only one subject had both serum Triglyceride and VLDL levels raised. These variations in parameters might be due to higher fat content of the last meal of the subjects, causing elevation which may be prolonged for several hours beyond the normal 8 hours required for clearance. The lowered HDL levels of the two cases might be due to their precancer status.

The p-values for lipid profile parameters when compared between the groups were – for TG p-value was 0.845, for TC p-value was 0.617, LDL Cholesterol p-value was 0.334, HDL Cholesterol p-value was 0.066 and VLDL Cholesterol p-value was 0.842. Therefore there is no significant difference in any of the parameters among the groups tested.

Discussion

Potentially malignant disorders, conveys that not all lesions and conditions described under this term may transform to cancer, rather, that there is a family of morphological alterations amongst which some may have an increased potential for malignant transformation. Potentially malignant disorders of the oral mucosa are indicators of risk of likely future malignancies elsewhere in (clinically normal appearing) oral mucosa and not only site specific predictors.13 The habit of tobacco consumption is a known etiological factor for the development of precancerous diseases and Oral Cancer.

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. This affects essential constituents of the cell membrane and might be involved in carcinogenesis/tumorigenesis. Due to the lipid peroxidation, there is a greater utilization of lipids including total cholesterol, lipoproteins and triglycerides for new membrane biogenesis. Cells fulfill these requirements either from circulation, by synthesis through the metabolism or from degradation of major lipoprotein fractions like VLDL, LDL or HDL. Lower blood lipids have been associated with various cancers. Furthermore, some investigators have also
found relation of low serum cholesterol with increased risk of cancer occurrence and mortality.¹

One of the objectives of the study was to assess the changes of serum lipid profile values of tobacco habit group when compared with the control group. On statistical evaluation, it was found that there was no significant difference in the serum lipid profile levels between the habit and the control groups. Hence no intra-group variability was further probed.

Another aim of our study was to assess variation of serum lipid profile values, if any, between habit group and precancer group. There was no significant variation of serum lipid parameters between the groups. This aim was undertaken so as to know that any change in the lipid profiling of the habit group subjects might be taken as an indication towards a precancer state.

This finding was not consistent with the study conducted by Phillips NR et al., (1981)² who found that the serum triglyceride, VLDL, LDL level increased and serum HDL levels decreased with the number of cigarettes smoked daily. The hypercholesterolemic state in tobacco users reported in a study conducted by Tucker LA (1989)³ was inconsistent with our findings.

The findings were also inconsistent with the studies conducted by Khurana M et al., (2000)⁴, Neki NS (2002)⁵ and Kshitiz KK et al., (2010)⁶ who found raised total cholesterol, LDL cholesterol, VLDL-cholesterol and, triglycerides and lowered HDL levels in tobacco users respectively. In a study conducted by Venkatesan A et al., (2006)⁷, who found raised total cholesterol and LDL levels in tobacco users, was inconsistent with our findings while the finding of no significant difference in HDL levels in the former study, was consistent with our study.

The findings of raised TC, LDL cholesterol and TG and lowered HDL cholesterol levels as compared to controls reported by Gupta BK et al., (2007)⁸ and Meenakshisundaram R et al (2010)⁹ in their study was not consistent with our findings. In the study conducted by Waqar A (2010)¹⁰ in Lahore city to evaluate the changes of the serum lipid profile in healthy adolescent male non smokers and smokers, no significant association was found in serum total cholesterol, VLDL levels, a finding consistent with our study while the reported finding of significant increase in serum triglyceride, LDL levels and significant decrease in serum HDL levels in smokers was inconsistent with our findings.

One of the aims of this study was to assess the variation, if any, in the serum lipid profile levels of precancer group when compared with the control group. We found that none of the serum lipid profile parameters significantly varied from that of the control group. Hence no intra-group variability was further probed.

These findings were consistent with the study carried out by Sugar L and Banoczy J (1969)¹² in patients in whom leukoplakia had been diagnosed sometime during the previous 23 years. In the three studies conducted by Dyer AR et al., (1981)¹³, there was no significant association between initial serum cholesterol level and subsequent mortality from cancer, or from causes other than cancer and the cardiovascular diseases in men. In the study when the cancer deaths were examined by site, there was a significant inverse association between serum cholesterol and deaths from sarcoma, leukemia and Hodgkin's disease. They also reported that serum cholesterol was not significantly related to lung cancer, colorectal cancer, oral cancer, pancreatic cancer, or to all other cancers combined in any of the three studies in men or in women. Thus, the results of these three studies do not generally support the hypothesis of an inverse association between serum cholesterol and cancer in urban middle-aged white American males and females. The results of this study were consistent with our findings.

In a study conducted by Alexopoulos CG et al.,(1987)¹⁴, it was reported that cancer patients (except breast cancer) as a group demonstrated significantly lower TC, esterified cholesterol and LDL cholesterol, compared with noncancer patients. Finally, the observed overall incidence of hyperlipidemia in cancer patients was not significantly different from the controls. Therefore the authors concluded that, either hypocholesterolemia is a secondary phenomenon to cancer process or its contribution to cancer development, if any causative relation exists, is very small. This study further supports our results that changes in serum lipid profile might not be associated with oral precancer status of the patient.

In a study conducted by Kritchevsky SB et al., (1991)¹⁵, they reported that cholesterol levels of the cases diagnosed with nonlocalized cancer dropped below the expected level approaching diagnosis when compared to the entire study population. No decrease was seen for those diagnosed with localized malignancies. Patterns for LDL cholesterol reflected those of total cholesterol. There was no clear relationship between cancer diagnosis and patterns of change for triglycerides and HDL cholesterol. This study further strengthened our results, as the oral precancers are lesions which affect mainly the oral...
cavity and, hence are localized, therefore, they might not cause any serum lipid profile variations.


Our results were consistent with the results of a study conducted by Nayak P et al., (2010)\(^6\), pertaining to the triglycerides and VLDL levels not showing significant variation, but not consistent pertaining to the reduced levels of total cholesterol, HDL and LDL in oral precancer group and also pertaining to the plasma TG and VLDL varying between OSMF and OLP cases. The results of a study conducted by, Lohe VK et al., (2010)\(^7\), was not consistent with our study pertaining to the decrease in total cholesterol and HDL levels in Oral Precancer group but consistent with no significant changes in other lipid profile parameters in Oral Precancer group and also with no overall significant correlation of serum lipid profile with tobacco abuse.

The possibility of not having any significant variation in serum lipid profiles of tobacco habit group and precancer group when compared with the control group can be explained by the following reasons- the subjects in the habit group might not have the long period of time of habit usage and the required frequency of habit which can represent the status that is at the verge of precancer conversion but without oral precancer manifestation and the patients in the precancer group in our study, as a group, might represent patients who are at an initial stages of precancer, which might not have caused the lipid changes in the blood.

A longitudinal study with long term follow up of cases with periodic estimation of lipid profile would be needed to establish correlation between a transformation from a precancerous state to malignancy.

References

Illustrations

Illustration 1

Graph 1: Graph Showing the sex-wise Distribution of the Groups

Illustration 2

Graph 2: Graph Showing the age-wise Distribution of the Groups
Illustration 3

Graph 3: Graph Showing the Serum Lipid Profile Comparisons Between the Groups

Illustration 4

Table 1: Table Showing the Mean of Serum Lipid Profile Comparisons Between the Groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>F</th>
<th>p-value</th>
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<td>Triglycerides</td>
<td>Cases</td>
<td>30</td>
<td>125.93</td>
<td>32.33</td>
<td>0.17</td>
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<td></td>
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<td>118.73</td>
<td>31.45</td>
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<td>Habit</td>
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<td>123.33</td>
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<td>29.19</td>
<td>0.49</td>
<td>0.617</td>
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<td>179.70</td>
<td>15.64</td>
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<td>186.20</td>
<td>29.60</td>
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<td>Cases</td>
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<td>15.97</td>
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<td></td>
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<td></td>
<td>Habit</td>
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<td>115.70</td>
<td>28.56</td>
<td></td>
<td></td>
</tr>
<tr>
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<td>Cases</td>
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<td>47.97</td>
<td>6.49</td>
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<td>0.066</td>
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</tr>
<tr>
<td></td>
<td>Habit</td>
<td>30</td>
<td>45.90</td>
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<td>VLDL</td>
<td>Cases</td>
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<td>6.46</td>
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<td>0.842</td>
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<td>Habit</td>
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