Alterations of Plasma lipid profile patterns in oral leukoplakia

N Mahesh¹, S A K Uroof Rahamathulla², Guntipalli M Naidu³, Amudala Rajesh¹, P Ravisekhar Babu³, J Muralinath Reddy⁴

Contributors:
¹Assistant Professor, Department of Oral Medicine & Radiology, KLR’s Lenora Institute of Dental Sciences, Rajahmundry, Andhra Pradesh, India; ²Assistant Professor, Department of Oral and Maxillofacial Surgery, C K S Theja Institute of Dental Sciences, Tirupati, Andhra Pradesh, India; ³Assistant Professor, Department of Public Health Dentistry, Drs. S & NR Siddhartha Institute of Dental Sciences, Chinnamangalam, Gannavaram, Andhra Pradesh, India; ⁴Reader, Department of Oral & Maxillofacial Pathology, C K S Theja Institute of Dental Sciences, Tirupati, Andhra Pradesh, India; ⁵Assistant Professor, Department of Conservative Dentistry, C K S Theja Institute of Dental Sciences, Tirupati, Andhra Pradesh, India; ⁶Assistant Professor, Department of Oral & Maxillofacial Surgery, Sri Sai Dental College, Srikakulam, Andhra Pradesh, India.

Correspondence:
Dr. Guntipalli M Naidu. Department of Public Health Dentistry, Drs. S&NR Siddhartha Institute of Dental Sciences, Chinnamangalam, Gannavaram – 521101, Andhra Pradesh, India. Phone No.: +91-9440787232. Email: naiduguntipalli@gmail.com

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Abstract:
Background: Oral cancer is associated initially by the presence of pre-malignant lesions or pre-malignant conditions. Oral leukoplakia is one of the best-known pre-malignant lesions in the oral cavity that have the highest rate of malignant transformation. Numerous studies have shown an altered lipid profile in various cancers including head and neck cancers. An inverse relationship between plasma lipid profiles have been seen in oral cancer and pre-cancerous subjects. The present study evaluated the plasma lipid profiles in oral leukoplakia and controls.

Materials and Methods: This study was done in department of Oral Medicine and Radiology, Sibar dental College and Konacc diagnostics. 30 patients were included in the study (15 patients with oral leukoplakia (histo-pathologically proven) and 15 patients for comparison of results as controls). Patients with cardiovascular diseases, uncontrolled diabetes mellitus, acute hepatitis and nephrosis were excluded from the sample and lipid profile assay was done by fully automated biochemistry analyser (EM–360). Paired-t and Scheffe tests were used to find statistical significance between two groups.

Results: The plasma lipid levels were estimated in between the two groups by arithmetic mean along with standard deviation. The lipid parameters included were Total cholesterol, HDL, LDL, VLDL, Triglycerides. The lipid parameters of the patients in between the two groups were compared and analysed.

Conclusion: In this study TC, HDL, LDL, Triglyceride level analysis showed slightly lower levels in oral leukoplakia patients than that of the controls. Higher VLDL levels were observed in leukoplakia than the control group.

Key Words: HDL, LDL, plasma lipid profiles, total cholesterol, triglycerides, VLDL

Introduction
Lipids are the major cell membrane components, which are essential for various biological functions like maintaining cell integrity, cell growth, and division of normal and malignant cells. Changes in the lipid profiles have been seen in various diseased conditions including the oral cancer. Numerous studies have shown an altered lipid profile in various cancers including head and neck cancers. An inverse relationship between plasma lipid profiles have been seen in oral cancer and pre-cancerous subjects. The lower plasma lipid status may be a useful indicator for initial changes occurring in neo-plastic cells.¹

In our present study, we evaluated the plasma lipid profiles in oral leukoplakia with the controls.

The oral cavity is the site of the body where contact with exogenous material, micro-organisms and harmful agents are more intense. The oral mucosa functions as a mechanical and immunological barrier. Protective mechanisms are noted in the form of increased capacity for epithelial regeneration and increased keratinisation. These epithelial changes are reactive and reversible but progressive loss of normal control mechanisms leads to pre-cancerous states and oral cancer. The concept of a two-step process of cancer development in the oral mucosa, i.e, the initial presence of a precursor subsequently developing into cancer, is well established. Oral leukoplakia is the best-known precursor lesion.²

Materials and Methods
This study was carried out in the Department of Oral Medicine and Radiology, Sibar dental College and Konacc diagnostics, Guntur, Andhra Pradesh. 30 patients were included in the study with 15 patients with oral leukoplakia and 15 healthy patients for comparison of results (controls).
Selection of cases
15 patients with Oral cancer (histo-pathologically proven) and 15 healthy individuals were included in the study. Patients with cardiovascular diseases, uncontrolled diabetes mellitus, acute hepatitis and nephrosis were excluded from the sample. (Figure 1 & 2)

Auto-analyser used for the analysis of the results are fully automated biochemistry analyser. (EM – 360) from Erba-Manheim.  

5ml of blood is collected from each subject and is allowed to clot and then the serum is separated by centrifugation. After that the lipid profile assay of the specific parameters like Total cholesterol, HDL, LDL, VLDL, Triglycerides were done.

Statistical Methods
In our present study the lipid parameters like Total cholesterol, HDL, LDL, VLDL, Triglycerides were statistically analyzed by paired- t test and Scheffe test to evaluate the significant proportion of lipid profile patterns between the two groups.

Results
In our present comparative study lipid parameters were estimated in two groups consisting of patients which included 15 patients with Oral leukoplakia as Group I, 15 patients as control group for comparison of results as Group II.

The oral Leukoplakia was distributed in various sites of oral cavity. In our study about 80% of the lesions were found on the buccal mucosa and commisures of the lip. Commisures of the lip was one of the most common site noted in India and rest of them were found on tongue (6.67%), palate (6.67%), gingiva (6.67%) respectively.  

(Graph 1)

The age distribution in group I was between 31 – 65 years with a mean age of 52.60 and standard deviation of 9.03. In

![Figure 1: Oral leukoplakia of commissure.](image1)

![Figure 2: Histo-pathological picture of leukoplakia showing epithelial dysplasia characterized by nuclear hyper-chromatism and pleomorphism.](image2)
Plasma lipid profile patterns in oral leukoplakia...Mahesh N et al

Group II the age distribution was between 19-65 years with the mean of 40.27 and standard deviation of 16.43 (Graph 2). Group I showed male predominance with almost 4:1 (m:f) ratio (Graph 3). Group II showed the ratio of 3:2. (Graph 3)

All the patients had deleterious oral habits like smoking, alcohol and tobacco chewing with betel nuts. About 53.3% of the patients had the habit of both Tobacco smoking mostly Beedi form (46.7%) and smoking along with Alcohol was seen in 53.3%.
The plasma lipid levels were estimated in between the two groups. The arithmetic mean along with standard deviation of all the parameters were calculated. The lipid parameters included were Total cholesterol, HDL, LDL, VLDL, Triglycerides. The abnormal lipid parameters of the patients in between the two groups were calculated and were as follows.
The changes in the total cholesterol level were compared by mean and standard deviation between Group-I and Group-II. The values were 147.87 and 45.09 in Group I patients and 183.73 and 24.28 in Group II with a P-value of 0.0492. (Table – 1)

Statistically significant changes in HDL levels were seen between Group I and Group II with a mean of 36.00 and standard deviation of 5.33 in Group I and with a mean of 44.27 and standard deviation of 6.28 in Group II. Pair wise...
Table 1: Comparison of two groups with respect to total cholesterol profile by Scheffe Test.

<table>
<thead>
<tr>
<th>Group</th>
<th>Means</th>
<th>Standard Deviation (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>147.87</td>
<td>45.09</td>
</tr>
<tr>
<td>Group II</td>
<td>183.73</td>
<td>24.48</td>
</tr>
<tr>
<td>Total</td>
<td>165.80</td>
<td>34.78</td>
</tr>
</tbody>
</table>

$I\text{-II} \quad 0.0492^*$

*Significant at 5% level of significance ($p<0.05$)

Comparison by Scheffe test between group I and group II was significant, with a $p$ value of 0.0433. (Graph 4)

Significant $p$ value of 0.0423 was seen in LDL profile comparison in between the two groups by Scheffe test between group I and group II. (Graph 5)

VLDL and Triglyceride profiles comparison in between the two groups by Scheffe test did not show significant $p$ values and many variations were not noted between the groups.

Discussion

Leukoplakia is the most common premalignant or potentially malignant lesion of the oral mucosa. The term
leukoplakia was derived from the Greek word Leuko - White and plak - plaque. The condition was first described by Bazin and others as a type of lingual psoriasis, but it was Schwimmer in 1877, who differentiated it from psoriasis and described it under the present name.\(^5\) Axell T et al in 1984 modified the definition of leukoplakia to “A whitish patch or plaque which cannot be characterized clinically or pathologically as any other disease and is not associated with any physical or chemical causative agent except the use of tobacco.”\(^6\)

The incidence and prevalence of leukoplakia vary in different parts of the world. In general the reported prevalence ranges from 0.2 to 0.5%, with remarkable regional differences. In India (0.2 – 4.9%), Sweden (3.6%), Germany (1.6%), Holland (1.4%).\(^7,8\) Leukoplakia is seen most frequently in the middle-aged and older men. Gender distribution is also variable. Male predominance is seen in different parts of India.\(^7\)

**Etiology**

The etiology of leukoplakia is still unclear. Even though various hypothesis have been put-forth, their association cannot be determined in most of the cases. Some workers believe that the initiation of this lesion may depend upon various predisposing factors.\(^9\) The factors most frequently thought to result in leukoplakia are tobacco, alcohol, virus, vitamin deficiency, candida, syphilis, galvanism, endocrine disturbances and local irritating factors.\(^10,11,12\) Although, tobacco seems to be the major inducing factor, many cases diagnosed does not have the habit of use of tobacco.\(^3,4,7\) Tobacco use may be either in the form of smoking/smokeless.\(^7\) 80% of leukoplakia patients are smokers.\(^10,11\) Polycyclic aromatic hydrocarbons aldehydes, aromatic amines, nitrosamines were thought to be carcinogenic components present in tobacco chewing. Tobacco with betel nuts increase the concentration of carcinogenic tobacco specific nitrosamine and reactive oxygen species in the mouth leading to the changes of the oral mucosa and resulting in the development of the lesion.\(^14\)

**Classification**

Wood and Goaz (1989) divided leukoplakia into four basic clinical appearances:\(^16\)

a. Homogenous: white plaques have no red component but have a fine white grainy texture or a more mottled rough appearance.

b. Speckled leukoplakia: white and red flecks of either fine or coarse variety.

c. Erythro-leukoplakia: A combination of white and red patches demonstrate segregation of the red and white components.

d. Verrucous leukoplakia: Red and white components in which white component is much thicker and so it protrudes above the surface mucosa.

William L.I.J (1990) divided leukoplakia clinically into two main types\(^17\)

a. Homogenous variety which carries low risk of malignant transformation.

b. Non homogenous variety which carries a higher risk which includes speckled leukoplakia comprising both red and white patches.

Proliferative verrucous leukoplakia is an aggressive type of leukoplakia that almost invariably develops into malignancy. This type is characterized by wide spread and multifocal appearance, often in patients without known risk factors.\(^18\)

**Clinical Features**

Leukoplakia can be either solitary or multiple. It may occur on any site of the oral cavity with the most common sites being the buccal mucosa, the commisures, lips, palate, maxillary mucosa, and the retro-molar area. Floor of the mouth and tongue are less likely sites. Approximately 50% of lesions affect the cheeks, mandibular mucosa and sulcus.

The lesions of the mouth and tongue is only one quarter as prevalent as lesions of buccal mucosa.\(^15\) On examination, patches of leukoplakia may appear white, gray or yellowish white but with heavy use of tobacco may assume a brownish yellow color. The surface of the lesion is often finely wrinkled or shrivelled in appearance and may feel rough on palpation. Patches of leukoplakia may vary from a non palpable faintly translucent white area to thick, fissured, papillomatous, indurated lesions.\(^12\)

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Pindborg JJ et al and Schepman KP et al have put forth the **Classification and Staging of Oral Leukoplakia as**\(^15\)

**Provisional (clinical) diagnosis**

L = extent of the leukoplakia

L1 = no evidence of lesion

L2 = lesion ≤ 2 cm

L3 = lesion 2-4 cm

L4 = lesion ≥ 4 cm
LX = not specified.
S = site of the leukoplakia
S1 = all oral sites, except for the floor of the mouth and the tongue
S2 = floor of the mouth and/or the tongue
Sx = not specified.
C = clinical aspect
C1 = Homogeneous
C2 = Non-homogeneous
Cx = Not specified.

Definitive (histopathological) diagnosis
P = histopathological features
P1 = No dysplasia
P2 = Mild dysplasia
p3 = Moderate dysplasia
p4 = Severe dysplasia
px = Not specified

Staging System for Oral Leukoplakia
Stage 1: any L, S1, C1, P1, or P2,
Stage 2: any L, S1, C2, P1, or P2
Any L, S, C, P, or P,
Stage 3: any L, S2, C2, P1, or P2,
Stage 4: any L, any S, any C, P3, or P4.

The lipids are a heterogeneous group of compounds known by their physical properties rather than by chemical properties. They serve as an efficient source of energy, as thermal insulator, and as important cellular constituents along with proteins both in cell membrane and in mitochondria within the cytoplasm. They serve as the means of transporting lipids in the blood.\(^1\)

Cholesterol and triglycerides are the important lipid constituents of cells and are essential for various physiological functions. Cholesterol is essential for maintenance of structure and functional integrity of all biological membranes and also important for stabilization of DNA helix.

The lipoproteins help in the transport of cholesterol and triglycerides in plasma as they are hydrophobic. The major functions of the plasma lipoproteins are transport of triglycerides and cholesterol from sites of synthesis to sites of storage, energy use or metabolism. The VLDL transports the endogenous synthesized triglycerides, LDL are the biologic vehicle to provide cholesterol to the peripheral tissues, HDL transports cholesterol from peripheral tissues to liver for degradation.\(^19\)

In our present study, the plasma lipid profile was estimated by the enzymatic method. The parameters that were considered were total cholesterol, High density lipoprotein cholesterol, Low density lipoprotein cholesterol, Very low density lipoprotein and Triglyceride levels. The total cholesterol level was slightly lower in Oral Leukoplakia patients than that of the controls with a P value of 0.0176. The inverse relation between the total cholesterol and disease stage and mortality was observed in various malignancies.\(^20\) Rywik SL et al in 1999 had shown a relatively high risk of cancer mortality with a significant lower total cholesterol as well as HDL. The lower level of TC was suggested due to increased utilization by tumor cells.\(^21\)

In our study a slight lower level was observed in plasma HDL in Oral leukoplakia than controls with a P value of 0.0411. This finding was in accordance with previous reports, that low HDL is an additional predictor of cancer. Patel et al stated that the lower HDL level may be a consequence of disease that is mediated by utilization of cholesterol for membrane biogenesis.\(^3\) Jacqueline et al observed a lower HDL in widespread disease than with localized tumors.\(^22\)

The range of LDL in oral leukoplakia patients was respectively lower than the controls. This lower level was not observed by Patel et al in head and neck malignancies. The lower level of cholesterol was noted in blood malignancies.\(^23\)

A significantly higher VLDL levels was observed in Oral Leukoplakia in our study than control group which was observed only in the breast cancer patients and was not inferred by malignancies of head and neck by Patel et al.\(^24\)

A significantly decreased Triglyceride levels was observed in leukoplakia patients than control group which was a similar finding as that of Patel et al.\(^1\)

Conclusion
In this study TC, HDL, LDL, Triglyceride level analysis showed slightly lower levels in oral leukoplakia patients than that of the controls. Higher VLDL levels were observed in leukoplakia patients than the control group.
These alterations in the plasma lipid profile patterns were significant and recommend a still in-depth study in this aspect for early diagnosis and management of oral leukoplakia to prevent malignant transformation.

References