ESTIMATION OF PLASMA LIPIDS IN DIFFERENT HISTOPATHOLOGICAL GRADES OF ORAL SQUAMOUS CELL CARCINOMA

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ABSTRACT

Background: Lipids play a major key role in maintenance of cell integrity. Since years there have been discussions about the correlation of alterations of the lipid profile and various cancers. Alterations in the lipid profile are associated with the oral cancer and oral precancer. Incidence of oral squamous cell carcinoma (OSCC) cancer has been reported to be more in patients with reduced lipid profiles. This study was done to evaluate the variation of plasma lipids in different histopathological grades of oral squamous cell carcinoma and to estimate the correlation of the altered lipid profile with tumor differentiation.

Methodology:
Blood samples from 30 oral squamous cell carcinoma patients (10 well differentiated, 10 moderately differentiated, 10 poorly differentiated) were subjected to lipid analysis. The lipid analysis was a panel of tests consisting of five main parameters; Total Cholesterol (TC), Triglycerides (TG), High Density Lipoproteins (HDLs), Low Density Lipoprotein (LDLs), and Very Low Density Lipoprotein (VLDLs). The results obtained were compared with the lipid profile of control group (n = 10). ANOVA test was done for correlating the lipid values.

Result & conclusion:
The results of ANOVA have shown significant values of TC, HDL and LDL with a ‘p’ value of 0.000, 0.000, 0.001 respectively. Hence Post Hoc Analysis was done to correlate among the control group, study group and various histopathological grades of oral squamous cell carcinoma. The results have shown no correlation among the grades of oral squamous cell carcinoma. Among the control group and oral cancer group the results were statistically significant. The “p” values of TG and VLDL were not significant with a value of 0.067 and 0.289 respectively. Since the results have shown no correlation among the histopathological grades of oral squamous cell carcinoma.

Overall, the results revealed that there is no significance in the variation of lipid levels between the histopathological grades of oral squamous cell carcinoma.

KEYWORDS
Histopathological, Oral Squamous Cell Carcinoma

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INTRODUCTION

Oral squamous cell carcinoma (OSCC) is the most common cancer worldwide. In India, among all cancers oral squamous cell carcinoma is the most common cancer in males and the third most common cancer in females.1 Oral squamous cell carcinoma can arise from pre-existing potentially malignant disorders, or de novo. The use of tobacco, betel quid, heavy drinking of alcoholic beverages and a diet low in fresh fruits and vegetables are the major risk factors for oral SCC.2 Its functional characteristics and morphological characteristics indicate the biological aggressiveness that is caused by the alteration and the mutation that alter the cell matrix interaction and cell signalling pathways.3 Squamous cell carcinoma is an epithelial malignancy that occurs in organs that are normally covered with squamous epithelium which includes several different anatomic sites, including the skin, lips, mouth, oesophagus, urinary tract, prostate, lungs, vagina, and cervix and is the most common cancer capable of metastasic spread.4 Approximately 15 to 20% of all oral cancer cases occur in patients without the traditional risk factors, reflecting in numerous cases of OSCC in non-smokers and non-alcoholic drinkers.5 One of the etiologic factor for such cases is Human Papillomavirus. While over 60 carcinogenic substances have been identified in tobacco smoke, the levels of known carcinogens are generally lower in smokeless tobacco, however, nitrosamines 4-(methyl nitrosamino)-1-(3-pyridyl)-1-butaneone (NNK) and N-Nitrosonornicotine (NNN) are present in both smokeless and inhaled tobacco products. NNK and NNN form covalent bonds with genomic DNA resulting in genomic instability and are thought to be the primary mediators of malignant transformation.6

Certain alterations in lipid metabolism can contribute to cancer development. It has also been detected that obesity is also one of the factor for cancer development. Lipids can promote different aspects of cancer development. Stimulation of fatty-acid synthesis by oncogenic signalling and increased mobilization from adipose tissue as a consequence of cachexia increase the availability of lipids in cancer cells. These may contribute to several aspects of the tumour phenotype, such as growth and proliferation, survival under oxidative and energy stress, support of a high-glycolytic rate by promoting redox balance and stimulation of signalling pathways that lead to proliferation and invasion.7

Lipid is an essential structural component of all cell membranes. It is present either as free cholesterol or combined with a long-chain fatty acid as cholesteryl ester in tissues and in plasma lipoprotein.8 Basically lipids are defined as a heterogeneous group of biomolecules that are generally insoluble in water but which readily dissolve in non-polar solvents, such as ether and chloroform.9 Lipids are high energy yielding molecules and include fats and oils, waxes, phospholipids,
steroids and some other related compounds. Fats and oils are made from two kinds of molecules: one glycerol and three fatty acids joined by dehydration synthesis known as triglycerides which are the major form of energy storage.10 Lipid metabolism connects to signalling networks in the regulation of cell growth, proliferation, differentiation, apoptosis and membrane homeostasis. Additionally, deregulated lipid metabolism can alter membrane composition and permeability which might cause the development and progression of many diseases especially carcinoma. Therefore, theoretically, lipid profiles in cancer cells could be distinguishable from those of normal cells, and such a distinctive lipid profile could be reflected in the biofluids of patients with oral squamous cell carcinoma. Lipidomics, describes the identification, quantification and profiling of individual lipid molecules extracted from biological samples. It has been widely utilized to diagnose and investigate the pathogenesis of various cancers, such as pancreatic adenocarcinoma, thyroid cancer, colon cancer, hepatocellular carcinoma, glioblastoma and prostate cancer. However few studies have been performed to systematically investigate plasma lipid profiling and to comprehensively characterize the changes in lipid metabolism between oral squamous cell carcinoma patients and controls. Phospholipids are the main lipids in the cell membrane, while triglycerides are stored as cell energy reservoirs. LDL, synthesized mainly in the liver, is transported in the blood stream for supplying triglycerides and cholesterol in cells experiencing an LDL receptor. HDL returns cholesterol mainly to the liver.11 Lipid profile assay forms one of the special investigations in most clinical biochemistry laboratories worldwide. The assay is becoming of increased importance in many countries because of increased cases of hypertension, diabetes mellitus, renal diseases, and other disease conditions. Lipid profile assay has found useful application in the monitoring of patients with diabetes mellitus and in the management of patients with Coronary artery disease, as well as malnutrition. It is used as a screening test in obese individuals, alcoholics and persons of high social status with the risk factors for cardiovascular diseases.12

This study will not only throw light on the lipid levels in different grades of oral squamous cell carcinoma but also increase the level of understanding as there are very little studies done comparing lipid levels with OSCC.

AIMS:
1. To estimate the plasma lipid levels in patients with oral squamous cell carcinoma
2. To compare and correlate the plasma lipid levels with various histopathological grades of oral squamous cell carcinoma.

OBJECTIVES:
1. Withdrawal of blood from the patients who were histopathologically confirmed with oral squamous cell carcinoma
2. Send for the analysis of lipid profile. The parameters included are TC, TG, HDL, LDL and VLDL

MATERIALS AND METHODS
Study design:
- The study was conducted in the Department of Oral Pathology and Microbiology, Yenepoya Dental and Medical College, Hospital Mangalore. The prior approval for conducting the study was obtained from the institutional Ethics Committee of Yenepoya (Deemed to be) University.

Methods of collection of data:
- The study included total of 30 individuals with oral squamous cell carcinoma patients who visited the Department of Oncology in Yenepoya Medical College from May 2018 to August 2018. 10 healthy controls were chosen from patients who visited the Department of Oral Medicine of Yenepoya Dental College.

Study group:
- Study groups were divided into three including
  - Group I: 10 well differentiated
  - Group II: 10 moderately differentiated
  - Group III: 10 poorly differentiated squamous cell carcinoma in each group.
- Control group:
  - 10 healthy controls were included in group IV

Inclusion criteria:
- Patients with histologically confirmed oral squamous cell carcinoma of various grades
- Healthy controls

Exclusion criteria:
- Patients with underlying systemic disease such as
  - Diabetes,
  - Hypertension,
  - Jaundice,
  - Kidney disorders or other systemic disease and malignancies elsewhere in the body
- ii. Patients on medication that alter the lipid levels

Methodology:
A thorough case history was taken and the procedure was explained to the patient. An informed consent was obtained from the patient (Anexure II). A biopsy was taken and after the due procedure the specimen was sent for the histopathological examination.

The tissue was then fixed in 10% formalin solution. The tissue was processed and cut by rotary microtome to obtain 5 micron paraffin sections. Each section was stained using haematoxylin and eosin. The diagnosis was given based on the various grades according to Broder’s classification.

The patients who were diagnosed as well differentiated, moderately differentiated and poorly differentiated oral squamous cell carcinoma (10 each) were recruited for the study. The patients were explained in detail about the study and the procedure they will be subjected to.

Blood samples were collected from oral squamous cell carcinoma patients. The blood was obtained by venous arm puncture. The area was cleared and made aseptic by using a disinfectant solution and dried. 3 ml of blood was drawn with the help of disposable syringe and 24 guage disposable needle transferred to a heparin bottle and send for lipid analysis.

Principle of the procedure for cholesterol:
The VITROS CHOL slide method is performed using the VITROS CHOL slides and the VITROS chemistry products calibrator kit 2 on vitros 250/350/950 and 5, 1 FS chemistry systems and the VITROS 5600 integrated system. The VITROS CHOL slide is a multilayered, analytical element coated on a polyester support. The method is based on an enzymatic method similar to that proposed by Allain et al. A drop of patient sample is deposited on the slide and is evenly distributed by the spreading layer to the underlying layers. The triton X100 (TX 100) surfactant in the spreading layer aids in dissociating the cholesterol and cholesterol esters from lipoprotein complexes present in the sample. Hydrolysis of the cholesterol esters to cholesterol is catalysed by cholesterol ester hydrolyase. Free cholesterol is then oxidised in the presence of cholesterol oxidase to form cholestene and hydrogen peroxide. Finally hydrogen peroxide oxidises a leuco dye in the presence of peroxidase to generate a coloured dye. The density of the dye formed is proportional to the cholesterol concentration present in the sample and is measured by reflectance spectrophotometry.

RESULTS
The present study was carried out to estimate various lipid profiles in OSCC and controls in a total of 30 OSCC patients and 10 controls.

Total participants were divided into four groups (n = 10 in each group) namely Group I, II, III and IV. Group I, II, III included well differentiated, moderately differentiated and poorly differentiated oral squamous cell carcinoma respectively and group IV included control groups. Venous blood was obtained from all the participants and was subjected to lipid profile analysis.

The statistical analysis for this study was ANOVA (analysis of variance). It is a collection of statistical models and their associated estimation procedures used to analyse the differences among group means in a sample.
TABLE 1: Correlation of the cholesterol parameters between the squamous cell carcinoma and the healthy control (mean value)

<table>
<thead>
<tr>
<th>LIPID PARAMETERS (mg/dl)</th>
<th>CONTROL</th>
<th>OSCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC</td>
<td>221.1</td>
<td>158.4</td>
</tr>
<tr>
<td>TG</td>
<td>142.3</td>
<td>199.4</td>
</tr>
<tr>
<td>HDL</td>
<td>51.1</td>
<td>28.4</td>
</tr>
<tr>
<td>LDL</td>
<td>45.7</td>
<td>94.9</td>
</tr>
<tr>
<td>VLDL</td>
<td>27.4</td>
<td>54.9</td>
</tr>
</tbody>
</table>

Mean values are showing mark difference among control groups and oral cancer groups. TC, HDL and LDL values are observed to be reduced in oral cancer groups whereas TG and VLDL values are increased in oral cancer groups. (Table 1).

TABLE 2: Comparing the cholesterol parameters with the various grades of squamous cell carcinoma (mean value)

<table>
<thead>
<tr>
<th>LIPID PARAMETERS (mg/dl)</th>
<th>WELL Differ</th>
<th>MODERATELY Differ</th>
<th>POORLY Differ</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC</td>
<td>184.0</td>
<td>151.2</td>
<td>140.1</td>
</tr>
<tr>
<td>TG</td>
<td>150.1</td>
<td>209.2</td>
<td>239.0</td>
</tr>
<tr>
<td>HDL</td>
<td>64.2</td>
<td>26.9</td>
<td>24.2</td>
</tr>
<tr>
<td>LDL</td>
<td>119.8</td>
<td>84.0</td>
<td>80.8</td>
</tr>
<tr>
<td>VLDL</td>
<td>30.2</td>
<td>32.6</td>
<td>41.8</td>
</tr>
</tbody>
</table>

Shows mean values of each lipid parameters in three different grades of oral cancer. The mean values of TC, HDL and LDL shows decrease in the value as there is decrease in the degree of differentiation. And it was also observed that mean values of TG and VLDL exhibited increase in the value with respect to decrease in degree of differentiation. Levels of TC, HDL and LDL are directly proportional to degree of differentiation and TG and VLDL are inversely proportional to degree of differentiation. (Table 2).

TABLE 3: ANOVA test to estimate TC levels

<table>
<thead>
<tr>
<th>Grades</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>95% Confidence Interval for Mean</th>
<th>ANOVA test p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WELL DIFFERENTIATED SCC</td>
<td>10</td>
<td>140.10</td>
<td>17.59</td>
<td>127.52 to 152.68</td>
<td>0.00  HS</td>
</tr>
<tr>
<td>MODERATELY DIFFERENTIATED SCC</td>
<td>10</td>
<td>151.20</td>
<td>27.41</td>
<td>131.59 to 170.81</td>
<td>0.00  HS</td>
</tr>
<tr>
<td>WELL DIFFERENTIATED SCC</td>
<td>10</td>
<td>184.00</td>
<td>50.60</td>
<td>147.80 to 220.20</td>
<td>0.00  HS</td>
</tr>
<tr>
<td>CONTROL</td>
<td>10</td>
<td>221.10</td>
<td>58.59</td>
<td>179.19 to 263.01</td>
<td>0.00  HS</td>
</tr>
</tbody>
</table>

TC values show high significance among the grades of squamous cell carcinoma and the control group.

TABLE 4: Post Hoc analysis of TC

<table>
<thead>
<tr>
<th>Bonferroni Dependent Variable</th>
<th>Treatment</th>
<th>Mean Difference</th>
<th>Std. Error</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>POORLY DIFFERENTIATED SCC</td>
<td>MODERATELY DIFFERENTIATED SCC</td>
<td>-11.10</td>
<td>1.800</td>
<td>1.000</td>
</tr>
<tr>
<td>WELL DIFFERENTIATED SCC</td>
<td>MODERATELY DIFFERENTIATED SCC</td>
<td>-43.90</td>
<td>2.500</td>
<td>0.001</td>
</tr>
<tr>
<td>WELL DIFFERENTIATED SCC</td>
<td>WELL DIFFERENTIATED SCC</td>
<td>-79.94</td>
<td>4.500</td>
<td>0.001</td>
</tr>
<tr>
<td>WELL DIFFERENTIATED SCC</td>
<td>CONTROL</td>
<td>-95.99</td>
<td>5.300</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Mean values are showing high significance among the squamous cell carcinoma and the healthy control. TC values show “high significance” in the results with the control.

TABLE 5: ANOVA test to estimate TG levels

<table>
<thead>
<tr>
<th>Grades</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>95% Confidence Interval for Mean</th>
<th>ANOVA test p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>POORLY DIFFERENTIATED SCC</td>
<td>10</td>
<td>239.00</td>
<td>57.91</td>
<td>176.11 to 301.89</td>
<td>0.006 NS</td>
</tr>
<tr>
<td>MODERATELY DIFFERENTIATED SCC</td>
<td>10</td>
<td>209.20</td>
<td>125.83</td>
<td>119.19 to 299.21</td>
<td>0.067 NS</td>
</tr>
<tr>
<td>WELL DIFFERENTIATED SCC</td>
<td>10</td>
<td>150.10</td>
<td>74.45</td>
<td>96.84 to 203.36</td>
<td>0.000  NS</td>
</tr>
<tr>
<td>CONTROL</td>
<td>10</td>
<td>142.30</td>
<td>56.88</td>
<td>94.45 to 190.15</td>
<td>0.000  NS</td>
</tr>
</tbody>
</table>

According to ANOVA test the rise in the value of TG has no significance among the grades and the control groups. Since there is no significance post hoc test has not been done.

TABLE 6: ANOVA test to estimate HDL levels

<table>
<thead>
<tr>
<th>Grades</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>95% Confidence Interval for Mean</th>
<th>ANOVA test p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>POORLY DIFFERENTIATED SCC</td>
<td>10</td>
<td>24.20</td>
<td>10.65</td>
<td>16.58 to 31.82</td>
<td>0.000  NS</td>
</tr>
<tr>
<td>MODERATELY DIFFERENTIATED SCC</td>
<td>10</td>
<td>26.90</td>
<td>4.28</td>
<td>23.84 to 29.96</td>
<td>0.000  NS</td>
</tr>
<tr>
<td>WELL DIFFERENTIATED SCC</td>
<td>10</td>
<td>34.20</td>
<td>9.89</td>
<td>27.13 to 41.27</td>
<td>0.000  NS</td>
</tr>
<tr>
<td>CONTROL</td>
<td>10</td>
<td>51.10</td>
<td>10.52</td>
<td>43.57 to 58.63</td>
<td>0.000  NS</td>
</tr>
</tbody>
</table>

It has been demonstrated that HDL value is showing high significance. Since the value shows the significance post hoc test has been done.

TABLE 7: Post Hoc Analysis of HDL

The above results have shown the significance between oral cancer and control. No significance among the various grades of SCC.

TABLE 8: ANOVA test to estimate VLDL levels

<table>
<thead>
<tr>
<th>Grades</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>95% Confidence Interval for Mean</th>
<th>ANOVA test p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>POORLY DIFFERENTIATED SCC</td>
<td>10</td>
<td>29.68</td>
<td>11.09</td>
<td>17.59 to 41.77</td>
<td>0.000  NS</td>
</tr>
<tr>
<td>MODERATELY DIFFERENTIATED SCC</td>
<td>10</td>
<td>34.57</td>
<td>12.09</td>
<td>22.58 to 46.56</td>
<td>0.000  NS</td>
</tr>
<tr>
<td>WELL DIFFERENTIATED SCC</td>
<td>10</td>
<td>41.27</td>
<td>13.09</td>
<td>29.28 to 53.26</td>
<td>0.000  NS</td>
</tr>
<tr>
<td>CONTROL</td>
<td>10</td>
<td>58.63</td>
<td>14.09</td>
<td>46.54 to 70.72</td>
<td>0.000  NS</td>
</tr>
</tbody>
</table>

It has been demonstrated that VLDL value is showing high significance. Since the value shows the significance post hoc test has been done.

TABLE 9: ANOVA test to estimate LDL levels

<table>
<thead>
<tr>
<th>Grades</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>95% Confidence Interval for Mean</th>
<th>ANOVA test p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>POORLY DIFFERENTIATED SCC</td>
<td>10</td>
<td>38.52</td>
<td>13.09</td>
<td>26.43 to 50.61</td>
<td>0.000  NS</td>
</tr>
<tr>
<td>MODERATELY DIFFERENTIATED SCC</td>
<td>10</td>
<td>43.57</td>
<td>14.09</td>
<td>31.48 to 55.66</td>
<td>0.000  NS</td>
</tr>
<tr>
<td>WELL DIFFERENTIATED SCC</td>
<td>10</td>
<td>41.27</td>
<td>15.09</td>
<td>29.18 to 53.36</td>
<td>0.000  NS</td>
</tr>
<tr>
<td>CONTROL</td>
<td>10</td>
<td>58.63</td>
<td>16.09</td>
<td>46.54 to 70.72</td>
<td>0.000  NS</td>
</tr>
</tbody>
</table>

It has been demonstrated that LDL value is showing high significance. Since the value shows the significance post hoc test has been done.
In this test it shows no significance among the grades of squamous cell carcinoma. But there is high significance among the control group and poorly differentiated OSCC, and control and moderately differentiated OSCC. Well differentiated OSCC shows no significance with the control group.

**TABLE 10: ANOVA test to estimate VLDL levels**

<table>
<thead>
<tr>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>95% Confidence Interval for Mean</th>
<th>ANOVA test p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lower Bound</td>
<td>Upper Bound</td>
</tr>
</tbody>
</table>

- **POORLY DIFFERENTIATED D SCC**: 10
  - Mean: 41.80
  - Std. Deviation: 20.25
  - 95% Confidence Interval: 27.32 to 56.28
  - ANOVA test p value: 0.289
  - ns

- **MODERATELY DIFFERENTIATED D SCC**: 10
  - Mean: 32.60
  - Std. Deviation: 21.19
  - 95% Confidence Interval: 17.44 to 47.76
  - ANOVA test p value: 0.102
  - ns

- **WELL DIFFERENTIATED D SCC**: 10
  - Mean: 30.20
  - Std. Deviation: 14.66
  - 95% Confidence Interval: 19.71 to 40.69
  - ANOVA test p value: 0.044

- **CONTROL**: 10
  - Mean: 27.36
  - Std. Deviation: 11.31
  - 95% Confidence Interval: 19.27 to 35.45
  - ANOVA test p value: 0.034

The reducing mean values among the various grades shows no significance as the "p" value is 0.289.

The inference from the above findings shows that alteration of the lipid parameters is highly significant among the control group and oral cancer group. The study also proves that the variation of the lipid parameters has no correlation with the tumor differentiation.

**DISCUSSION**

Oral squamous cell carcinoma is the most common malignancy of the oral cavity accounting for 95% of all oral malignant lesions. Tongue, floor of the mouth, buccal mucosa and inferior lips are mostly affected. Palate is a rarely affected site.13 Etiology of oral cancer is certainly multifactorial, including smoking, tobacco, arecanut, betel quid. Nowadays viruses also have been demonstrated as a factor for malignancy.14 It has also been noticed that tobacco consumption can lead to the development of potentially malignant disorders that can show a high significant tendency to develop cancer.15 A genetic predisposition has also been suggested, due to the fact that the majority of the population exposed to these risk factors do not develop oral cancer, as well as the fact that sporadic cases of oral tumors occur in young adults and non-users of tobacco and alcohol.

Despite of the development of the recent advances in multimodal treatment regimes, the prognosis of oral squamous cell carcinoma is still poor. This happens because the symptoms that indicates the presence of the carcinoma appear when the tumor is in advanced stage. Because of such problems it is very useful to find biochemical markers that allow to suspect the presence of carcinoma at early stages.16 There are many biochemical markers available for precancer and cancer out of which lipid profile is a very important biochemical markers since carcinogenesis has also shown alteration in the lipid levels.17

Lipids comprise a heterogeneous group of compounds of biochemical importance. Lipids may be defined as compounds which are comparatively insoluble in water. Lipids are freely soluble in nonpolar organic solvents like chloroform, benzene, ether, alcohol etc.17 Cholesterol and triglycerides are imperative lipid components of cell and are critical in carrying out necessary physiological functions. It is necessary for structural and functional cell integrity.18 In the cell membrane phospholipids are the main lipids and triglycerides are considered as energy reservoirs.11 Lipids need help of carriers in plasma since they are insoluble in water hence lipids are complexed with proteins to form lipoproteins. The protein part of lipoprotein is known as apolipoprotein. By ultra centrifugation, depending on the density lipoproteins are classified into five types: Chylomicrons, formed in the intestinal mucosal cells and secreted into lacteals of lymphatic system; Very low density lipoprotein (VLDL) synthesized in liver and carries triglycerides from liver to peripheral tissues for energy needs; Low density lipoprotein (LDL) which is also known as bad cholesterol transports cholesterol from liver to peripheral tissues; High density lipoprotein (HDL) or good cholesterol that helps in transportation of cholesterol from peripheral tissues to liver.

The exact role of these metabolic alterations in the development and maintenance of the disease is not fully understood.19 Higher rate of cancer cell proliferation requires rapid synthesis of lipids for the biological process. De novo lipogenesis is considered to be the initial source of fatty acids available for lipid synthesis in cancer cells. De novo lipogenesis provides cancer cells with membrane building blocks, signaling lipid molecules, posttranslational modifications of proteins as well as energy supply to support rapid cell proliferation. First, quite a number of endogenously synthesized fatty acids are esterified to phospholipids, which provide pivotal structural lipids, facilitating the formation of detergent-resistant membrane microdomain for signal transduction, intracellular trafficking, polarization, and migration required for cancer cells. Second, the newly generated lipids molecules, such as phosphatidic acid (PA), diacylglycerol (DAG), and lysophosphatidic acid (LPA), also mediate signal transduction in cancer cells. These lipids regulate a variety of cellular functions including cell proliferation, survival and migration by either activating other signaling proteins inside the cells, or binding to a series of G protein-coupled receptors (GPCRs) on the cell surfaces. Third, the post-translational protein modification with lipid is also a vital process in regulating expression, localization and function of various signaling proteins. Phosphatidylinositol (PI)-associated modification through a carbohydrate linker to the proteins (GPI-anchored proteins) directs them toward to cell surface from endoplasmic reticulum (ER). Some GPI-anchored proteins, such as urokinase-type plasminogen activator (uPA)-receptor (uPAR) and membrane anchored serine protease matriptase (also known as MT-SP1 and epithin), have strong association with cancer. The lipid coordinated modification of Hedgehog and Wnt, two important signal molecules, regulates their signaling capacity and secretion. The lipidation controls the trafficking of Ras GTPases among ER, Golgi and plasma membranes and determines the signaling outputs. Finally, in response to glucose limitation, fatty acid can also be consumed through oxidation to provide key substitute energy for cancer cell survival. It is reported that stimulation of fatty acid oxidation is sufficient to maintain cell survival and protect cells from glucose withdrawal-induced death inAkt-overexpressing glioblastoma. In some types of cancers, such as prostate cancer, fatty acid oxidation is proposed to be a dominant bioenergetic pathway.20
lipid peroxidation product, malondialdehyde, may cross-link DNA through adenosine and cytosine and this cross-linking may result in carcinogenesis and mutagenicity.

In our study we infer that the reduction of TC was because of onco genesis or high activity of LDL receptors, reduced value of HDL is because of increased utilization of cholesterol for membrane biogenesis of the highly proliferating malignant cells and LDL is more susceptible to oxidation. TG and VLDL have shown slight increase in the values. The rise in the value of TG is unknown and VLDL is not related to oncogenesis.

In the present study a correlation of lipid profile was done only with histological grades of squamous cell carcinoma. We did not take clinical staging or the size of the primary tumour in to consideration. Since the reduction in lipid profile values in carcinomas are primarily linked to the utilization of lipid by cancer cells, the tumour size may have a significant influence on the values. Furthermore the lipid profile of the patients prior to development of the oral cancer was also not recorded. Further studies including these parameters in larger study groups will improve the insight about lipid profile in oral cancer patients.

CONCLUSION
The present study was carried out to estimate the lipid profile in oral squamous cell carcinoma patients and to correlate the findings between different histological grades of the same. From this study following conclusions can be made:

1. TC, HDL and LDL is lower in oral squamous cell carcinoma patients compared to healthy controls indicating TC was because of onco genesis or high activity of LDL receptors, reduced value of HDL is because of increased utilization of cholesterol for membrane biogenesis of the highly proliferating malignant cells and LDL is more susceptible to oxidation.
2. TG and VLDL were higher in oral squamous cell carcinoma patients The rise in the value of TG is unknown and VLDL is not related to oncogenesis.
3. No significant difference was observed between different grades of squamous cell carcinoma. High significant differences were noted among the control and cancer group proving that the cellular and the architectural changes from the normal to malignant phenotype leads to alteration in the lipid levels. The tumor differentiation has no role in the alteration of the lipid levels.

REFERENCES
10) Chawda JG, Jain SS, Patel HR, Chaudhula N, Patel K. The importance of lipids in malignant tumors provides the knowledge on membrane constituents of proliferating cells and signalling pathways that drive tumorigenesis. Another hallmark of cancer is dysregulation of cholesterol. Cholesterol is an essential factor for heart disease and now it has become the focus of attention. Several prospective and retrospective studies have been carried on plasma lipids on oral cancer and have observed an inverse relation in oral cancer patients. A recent addition is that lipid peroxidation may play an important role in cancer development as lipids, proteins, DNA, etc. Tobacco induces generation of free radicals and reactive oxygen species responsible for high rate of oxidation/ peroxidation of polyunsaturated fatty acids (PUFA), in turn leading to increased utilization of lipids. Lipid peroxidation may play an important role in cancer development as lipid peroxidation product, malondialdehyde, may cross-link DNA through adenosine and cytosine and this cross-linking may result in carcinogenesis and mutagenicity.

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