Original Article

# Oral Cancer: Correlation of Histopathological Grading and Location with Lipid Profile

Lipid profile as Biomarker in Oral Cancer

**Sanaa Ahmed[1], Hira Tariq[3], Uzma Naseeb[4], Ruqaya Shah[5], Maria Naz[1] and Muhammad Atif[2]**

## ABSTRACT

**Objective:** To compare the level of HDL, LDL, Triglycerides and Cholesterol in OSCC patients with that of healthy individuals and to find out the relationship between the level of HDL, LDL, Triglyceride and Cholesterol with location and histopathological grading of the tumor.

**Study Design:** Prospective Case-Control study

**Place and Duration of Study:** This study was conducted at the OPD of Jinnah Postgraduate Medical Center and Sindh Institute of Oral Health Sciences, from July, 2018 to December, 2019 for a period of one and a half year.

**Materials and Methods:** Sample size of 24 controls and 24 cases was calculated through open epi keeping in consideration Odds ratio of 7.1% from previous studies.

**Results:** LDL, HDL and Triglyceride levels increased while HDL decreased in Oral cancer patients in comparison to controls. We also compared the lipid profile levels with histopathological differentiation and location of the lesion finding out that the well differentiated tumor has lipid values within normal range except for LDL levels which becomes opposite in poorly differentiated squamous cell carcinoma.

**Conclusion:** Our findings are concurrent with previous studies that lipid profile varies with malignant transformation in oral cancer. Longitudinal studies are required to provide a definite conclusion on the matter.

**Key Words:** Mouth Neoplasms, Cholesterol, Cell Differentiation, Lipoproteins; LDL, Smokeless Tobacco

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## INTRODUCTION

According to WHO statistical report 2014 Head and Neck cancers are ranked the 7th for the incidence and 9th for causing deaths [1]. It has the highest incidence in Papua New Guinea, Bangladesh, Hungary, and Sri Lanka. Oral cancer due to the chronic use of Pan, Betel nut and Gutka is at its peak in the Sub-continent. Incidence in Pakistan is around 4.1%, which is very high [2]. Treatment outcome is dependent upon early detection and locoregional spread. Both factors directly affect the mortality and morbidity rate. As a result, there is a negative impact on the quality of life of these patients [3].

[1.] Department of Oral Medicine / Oral Pathology[2], Sindh Institute of Oral Health Sciences, Jinnah Sindh Medical University, Karachi.

[3.] Department of APPNA Institute of Public Health / Biochemistry[4] / Oral Maxillofacial Surgery[5], Jinnah Sindh Medical University, Karachi.

Correspondence: Dr. Sanaa Ahmed, Sindh Institute of Oral Health Sciences, Jinnah Sindh Medical University, Karachi.
Contact No: 0333-9533076
Email: drsanaaumair@gmail.com

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Lipids are essential for the normal biological functions in the human body. It is part of cell growth and multiplication. In oral cancer, lipid peroxidation due to free radical formation occurs which affects the cell cycles [2-4]. Dividing cells require lipids for growth and expansion [2-4]. Hence, the current trend for finding out the link between lipid levels and their association with oral cancer (since cancer cells are also rapidly dividing and multiplying). Plus, lipid profile levels are commonly prescribed, cheap, and non-invasive tests, which could increase the chances of early detection improving the outcome of these patients. There are several studies on correlation of lipid profile with Oral squamous cell carcinoma incidence and prognosis. Still there is no data on correlation of histopathology grading and derangement of lipid profile according to age and gender. Also, obesity was recently added to the list of the risk factors for cancer [2].

Lipid profile in patients with oral squamous cell carcinoma and premalignant lesions was studied in 2014 by Rahul Mehta [3]. He observed decline in Triglycerides, LDL, HDL and VLDL in comparison to control groups. The same was shown in previous studies [4-13].

The relation is inverse between malignancy and plasma lipid levels. Still the stigma remains whether this effect is the cause or the effect of carcinogenesis [14]. There are still to date few studies on oral cancer and lipid profile as biomarkers. The aim of the study is to evaluate the

levels of serum plasma lipids in patients of oral cancer and to correlate it with the severity of the disease. This will not only provide a cheap but also a less invasive, early detection test for oral cancer.

# MATERIALS AND METHODS

A prospective case-control study was conducted through data of patients coming to the dental OPD of Sindh Institute of Oral Health Sciences and Jinnah postgraduate medical center diagnosed with oral cancer from July 2018-Dec 2019. Data collection was through convenient sampling. The "Case group" included all the diagnosed oral cancer patients who have not started treatment. Diagnosis was based on a histopathological report confirming dysplasia or cancer. "Healthy controls" were selected matching age and sex of the patients in "Case group" keeping ratio of 1:1. For the collection of data, 2 proformas were used, one for the control group and the other for the cases group.

**Data Collection Process:** Samples were recruited from the dental outpatient departments after taking consent and agreeing on getting tested for Lipid profile. All samples were sent to the JPMC lab so that the results are under uniform conditions. They were required to give 5 ml blood after 8-10 hours of Fasting.

**Inclusion Criteria:** Patients aged between 20-65 years with no history of chemo or radiotherapy or medical history of hypertension, diabetes mellitus, triglyceridemia, liver, renal and coronary heart disease, obesity or with family history of hyperlipidemia and pregnancy were included.

**Sample Size Calculation:** The sample size of 24 healthy and 24 controls was calculated using the software Open Epi with Odds Ratio of 7.1 for chewing tobacco and risk of oral cancer from previous studies is taken keeping 95% confidence level and bound on error of 5% [13].

**Lipid test details:** All the patients who fulfilled the criteria and consented to be part of the study were asked to take Lipid profile test at JPMC laboratory to keep the results under uniform conditions. Five milliliters of fasting blood sample (8–10 h) was collected under aseptic conditions.

# RESULTS

Statistical analysis through SPSS version 17 was done. Mean and standard deviation of variables based on histopathological differentiation was calculated in Table 1. It shows mean and standard deviation with standard deviation of error was calculated for both groups that are healthy controls and cases. On comparison of the data, cases have more standard deviation in their data set for LDL, Cholesterol, and triglyceride while in healthy controls only high variation is seen in HDL levels. Though, for both cases and healthy controls, the standard deviation and mean values for LDL, HDL, cholesterol, and triglyceride are not far off but standard deviation is double in LDL level in "case group" in comparison to "healthy controls".

**Table No.1: Comparison Lipid Profile between Patients & Normal Individuals**

| Lipid Profile. | Groups | |
|---|---|---|
| | Cases (Means ± SD) | Healthy (Means ± SD) |
| LDL | 100.78 ± 62.381 | 97.57 ± 32.331 |
| HDL | 55.86 ± 21.859 | 27.22 ± 14.687 |
| Cholesterol | 174.22 ± 68.461 | 126.14 ± 66.867 |
| Triglycerides | 136.00 ± 46.704 | 95.00 ± 35.511 |

In Table 2 and 3 shows the correlation of lipid profile with location and histopathological grading of tumor. The results suggest that lipid profile does change in cancer patients relative to healthy individuals and they also are affected by the level of histopathological differentiation.

**Table No.2: Variation of Lipid Levels according to Histopathological differentiation of lesion**

| Histopathological Differentiation | LDL | HDL | Cholesterol | Triglyceride |
|---|---|---|---|---|
| Poorly Differentiated | Normal | Decreased | Decreased | Decreased |
| Moderately Differentiated | Normal | Decreased | Normal | Increased |
| Well Differentiated | Increased | Normal | Normal | Normal |

*Reference range (John Hopkins Hospital)[35]
LDL= < 100 mg/dL
HDL= ≥ 40 mg/dL
Cholesterol = < 200 mg/dL
Triglycerides = <150 mg/dL

**Table No.3: Variation of Lipid Levels according to the Location of Lesion**

| Site | LDL | HDL | Cholesterol | Triglyceride |
|---|---|---|---|---|
| Buccal Mucosa | Increased | Normal | Normal | Normal |
| Tongue | Increased | Decreased | Normal | Increased |
| Alveolus | Normal | Decreased | Increased | Increased |

*Reference range (John Hopkins Hospital) [35.]
LDL = < 100 mg/dL
HDL = ≥40 mg/dL
Cholesterol = < 200 mg/dL
Triglycerides = <150 mg/dL

# DISCUSSION

Oral cancer is on the rise in Pakistan [14]. Second leading cause of death in 2020 was Cancer. According to the World Health Organization cancer caused 9.6 million deaths in 2018. Tobacco use was one of the most common risk factors contributing to 22% of the cancer deaths[15]. Early diagnosis improves the prognosis and quality of life of the patients suffering from cancer. Especially in third world countries where resources are less, finding a cheap, non-invasive, and *commonly* available test can expedite early diagnosis and overall living conditions. Recently, there is a rise in utilizing complete blood count and lipid profiles in diagnosing

cancers of other areas such as breast cancer, colon cancer, ovarian cancer and they are found to be effective in doing so [16]. These studies found an inverse relationship between lipid profile and malignancy [16].

The etiology explained behind the decreasing level of lipid in serum is due to excessive degradation of the lipid compounds to divide and grow by both normal and cancerous cells [17]. Hypocholesteremia is taken as a risk factor for developing tumors. Maintaining the level of lipid profile to diagnose and treat several diseases has been suggested and explored by several researchers. In previous literature the results are varied but mostly quote that the HDL, LDL, Triglyceride, Cholesterol and VLDL decreases in cases of Oral cancer in comparison to healthy controls [4-13,18-29]. One study showed no change in lipid profile of Oral cancer patients in comparison to controls [30]. While few studies reported increase in lipid profile in cases of Oral cancer [31-34]. Our findings are consistent with increase in LDL, Triglyceride, cholesterol level in oral cancer patients though HDL was relatively low in comparison to Healthy controls (Table 1)[32-34].

We also correlated the histopathological differentiation with different lipids. We found that well differentiated showed an increase in LDL levels while the rest remained in normal range (Table 2) whole moderately differentiated showed decrease in HDL level and increase in Triglyceride levels while LDL and Cholesterol reading were within normal range. The poorly differentiated tumor showed a completely opposite picture of the well differentiated one. In previous studies failed to find any link between the two [11,16,27]. Further studies are required to explore these findings.

We also compared the lipid levels according to the site of the pathology in Table 3 and found that Alveolus and Buccal mucosa tumors had normal HDL levels. LDL levels increased in tongue and buccal mucosa while remaining within normal range in alveolus tumors. Cholesterol levels increased in Alveolus tumors while remaining in normal range in buccal and tongue cancers. Triglycerides were in normal range in buccal mucosa while increased in alveolus and tongue tumors. Prior studies did not show any pattern in lipid profile levels with change in the site of the tumor [11,16,27].

Longitudinal studies comparing the changes in lipid profile from early signs of change, premalignant lesion, or condition to development of malignancy should be designed if lipid profiles are to be utilized in future for early diagnosis and as part of supportive therapy during treatment phase. Sample size should be large enough to support or refute previous findings. Also, studies would also explore comparing data of patients on antihyperlipidemic medications developing OSCC with patients having no comorbid.

# CONCLUSION

Our findings are concurrent with previous studies that lipid profile varies with malignant transformation in oral cancer. Longitudinal studies are required to provide a definite conclusion on the matter.

**Author's Contribution:**

| | |
|---|---|
| Concept & Design of Study: | Sanaa Ahmed |
| Drafting: | Hira Tariq, Uzma Naseeb |
| Data Analysis: | Ruqaya Shah, Maria Naz, Muhammad Atif |
| Revisiting Critically: | Sanaa Ahmed, Hira Tariq |
| Final Approval of version: | Sanaa Ahmed |

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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