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Serum lipid profile in oral squamous cell carcinoma: alterations and association with some clinicopathological parameters and tobacco use

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Abstract. Hypocholesterolemia has been observed in patients with cancers of various organs; however the potential role of alterations in serum lipid profile in oral cancer remains controversial. Hence, this study aimed to evaluate the serum lipid profile in oral squamous cell carcinoma (OSCC) and its prognostic significance. Ninety untreated OSCC patients, who reported to the craniofacial unit for treatment between 2011 and 2014, were identified to obtain clinicopathological data and preoperative blood investigations including lipid profile. The fasting blood lipid profile, including total cholesterol (TC), triglyceride (TG), high density lipoprotein (HDL), and low density lipoprotein (LDL), was evaluated using a fully automated biochemistry analyser. Data were analyzed statistically using the Student's *t*-test, analysis of variance, and post hoc tests. Statistically significant decreases in serum TC, HDL, and LDL levels were observed in OSCC patients as compared to healthy controls ($P < 0.05$). There was no statistically significant difference in mean lipid profile values in terms of stage, grade, or lymph node metastasis. This study identified changes in lipid profiles in OSCC. The results suggest that during the development and progression of OSCC, levels of serum lipids are decreased. A review of the literature confirmed that OSCC patients exhibit aberrant serum lipid patterns.

Key words: oral squamous cell carcinoma; tumour stage; histological grade; lymph node status; serum lipid profile; tobacco abuse.

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Oral cancer is the eighth most common cancer in the world.[1] In India, oral cancer is the second most common cancer.[2] Squamous cell carcinoma (SCC) comprises about 90–95% of all oral malignancies, and hence the term 'oral cancer' is used in a restricted sense to describe SCC.[1] The mechanism of carcinoma development is complex and comprises proliferation, apoptosis, and differentiation, and the interplay between these intricate processes determines tumour development and

progression.[3] Newly proliferating tumour cells need many of the basic components used in physiological processes at well above the normal limits. An example is the lipids that form the major cell membrane components essential for various biological functions, including cell division and the growth of normal and malignant tissues. The increased need for lipids to fulfil the requirements of these new cells would be expected to diminish the existing lipid stores.[4] Also, cancer cells that are not rapidly proliferating require increased amounts of lipids for enhanced signalling and resistance against apoptosis.[5]

Oral cancer may interfere with food intake, therefore it can be intuitively expected that patients with oral cancer will have lower serum levels of lipids because of lowered lipid digestion and absorption. However, the plasma cholesterol concentration is not simply derived from dietary cholesterol intake or endogenous cholesterol. Rather, it also reflects the rate of synthesis of cholesterol-carrying lipoproteins. Therefore, serum lipid levels are less influenced by oral intake, and other factors such as genetic background or hormones, or environmental issues, are also involved in the regulation of plasma cholesterol.[5,6]

The utility of variations in blood cholesterol levels in the diagnosis and treatment of various diseases has been studied by several researchers.[7] High cholesterol levels in the blood are associated with an increased risk of coronary heart disease, whereas the implications of decreased cholesterol levels remain imprecise.[7,8] Researchers have reported the association of plasma/serum lipids and lipoproteins with different cancers.[4] Cancer patients often display significantly lower levels of serum total cholesterol (TC).[9] An inverse association between cholesterol and all cancers, such as hematopoietic, bowel, lung, prostate, and head and neck cancers, as well as oesophageal cancers, have been reported in the literature.[7,10,11] The 'preclinical cancer effect' hypothesis has received considerable attention as an explanation for the observed inverse association. Malignant neoplasms are known to have protean physiological effects, which might include the depression of blood cholesterol.[10] Some investigators have also found a relationship between low serum cholesterol and an increased risk of cancer occurrence and mortality.[12–14] Alterations in the circulatory cholesterol levels have been found to be associated with the aetiology of breast cancer and colorectal cancer.[15,16] Breast cancer patients display significantly elevated levels of serum cholesterol, and a few studies have shown high cholesterol levels to be associated with an increased risk of breast cancer and cancer recurrence.[17–19] However, the literature on the cancer–cholesterol question has remained inconsistent.[5,10]

Studies have demonstrated that cancer patients often display aberrant lipid profiles. The association of different lipoprotein sub-fractions with cancer risk has also been studied widely.[5] Low levels of serum high density lipoproteins (HDL) have been associated with an increased risk of all cancers.[9,20] In contrast, other studies have shown an increased risk of cancer associated with high levels of serum HDL.[5] Patients with breast cancer display high levels of HDL in comparison with healthy individuals.[21] Decreased serum low density lipoprotein (LDL) levels have also been shown to be associated with an increased risk of various cancers.[9,20] However, increased LDL levels have been associated with an increased breast cancer risk.[17,18] Serum triglycerides (TG) are significantly elevated in all types of cancer, as demonstrated by various studies.[5,9,18] Serum lipid levels of cancer patients also fluctuate during chemotherapy, and levels may return to normal after treatment. These observations corroborate the correlation between an abnormal serum lipid profile and disease activity.[5]

Significantly lower levels of serum cholesterol, HDL, LDL, and TG have been noted in the majority of studies on oral cancer.[8,22,23] Others have observed no significant differences in serum lipid fractions, or a significant increase in the levels of lipid fractions.[24–26] This information points to an irregular lipid pattern in oral cancer patients. Although alterations in serum lipid profile patterns have long been associated with malignancies, the role of these alterations remains controversial. There is debate as to whether hypocholesterolemia is a predisposing factor for cancer development, or hypocholesterolemia is in fact the result rather than the cause of cancer.[4]

Some studies have reported alterations in serum lipid profiles in oral precancer and oral cancer,[8,26,27] but have included small samples. The present study was performed on a relatively large cohort of OSCC patients, comparable to certain earlier research.[6,7,11,28] This study aimed to compare and correlate the serum lipid profiles of patients with carcinoma of different stages and grades, to compare and correlate serum lipid profiles in nodal metastatic and non-metastatic patients, and to determine the association with tobacco consumption.

Methods

A total of 120 patients ranging in age from 20 to 75 years were included in this hospital-based case–control study. Approval for the study was obtained from the ethics committee of the institute. After obtaining written informed consent from the participating patients, a thorough clinical history was taken, including height and weight (to calculate body mass index) and the type, form, frequency, and duration of tobacco use. The subjects were divided into two groups.

Group I consisted of 90 untreated OSCC patients, reporting to the craniofacial unit of the institution for treatment (excision of the lesion along with neck dissection) during the years 2011–2014. The patients were diagnosed with OSCC based on clinical and histopathological examinations. Staging was done according to the Union for International Cancer Control (UICC) classification. Along with the complete blood investigation performed routinely prior to surgery, the patient's preoperative fasting blood lipid profile was also evaluated. The subjects in the OSCC group were further classified into tobacco users (TU) and non-tobacco users (NTU). Differences in lipid profiles for the various types of tobacco use, i.e. smokeless tobacco, smoking tobacco, and a combination of both forms, were also analyzed.

Group II included 30 age- and sex-matched healthy individuals attending the institution for a routine dental check-up and treatment, without any history of tobacco abuse or oral lesions. These subjects were selected randomly amongst the people who visited the same hospital during the same time period. All of the selected control subjects had a similar socioeconomic background and similar quality of diet to the cancer cases.

Exclusion criteria

Patients who were obese, had any form of cardiac, renal, or liver disorder, uncontrolled diabetes, hypertension, or thyroid disorders, those who were pregnant, patients with a family history of hyperlipidemia, those receiving lipid-lowering drugs, patients on chemotherapy or radiotherapy, and those with malignancies elsewhere in the body were excluded from the study.

Analysis of the lipid profile

A 5-ml blood sample obtained in a fasting state was collected under sterile conditions in a plain vacutainer and allowed to clot