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EVALUATION OF SERUM LIPID PROFILE IN PATIENTS WITH ORAL POTENTIALLY MALIGNANT DISORDERS AND ORAL SQUAMOUS CELL CARCINOMA -A CASE CONTROL STUDY

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ABSTRACT

Lipids are the major cell membrane components, which are essential for various biological functions, such as maintaining cell integrity, cell growth, and division of normal and malignant cells. 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. It has been suggested a causative relationship might exist between plasma lipid levels and oral cancer patients. Further, the habit of tobacco consumption is on the rise and most often the oral cancer patients are afflicted with this menace. This study is conducted to understand the role of these lipids in the oral potentially malignant disorders like Oral Leukoplakia, Oral Submucous fibrosis and also in Oral Squamous Cell Carcinoma. A total number of 75 patients were involved in the study An inverse relationship exists between serum lipid profile in Oral cancer and Oral Potentially Malignant disorders. The lower serum lipid status may be a useful indicator for initial changes occurring in neoplastic cells

KEYWORDS: Lipid, Oral Cancer, Oral Potentially Malignant Disorders.

INTRODUCTION

Oral cancer is the sixth most common cancer worldwide and continues to be the most prevalent cancer related to the consumption of tobacco, arecanut, alcohol and other carcinogenic products.

Several studies have shown clearly that oral cancer usually preceded by Potentially malignant disorders. A precancerous lesion is defined as a morphologically altered tissue in which cancer is more likely to occur than in its apparently normal counterpart, and oral precancerous condition is defined as the generalized state associated with increased risk of cancer. Leukoplakia, erythroplakia, palatal changes among reverse smokers are premalignant lesions whereas oral lichen planus and oral submucus fibrosis are premalignant conditions.[1]

Leukoplakia is defined as a white patch or plaque that cannot be characterized clinically or pathologically as any other disease. Factors most frequently blamed are tobacco, alcohol, oral sepsis, local irritation, syphilis, vitamin deficiency, endocrine disturbances, galvanism, and actinic radiation in the case of the Leukoplakia of the lips. Tobacco has been cited as the most frequent offending agent. Leukoplakia is more common in men than in women, and is seen chiefly in the older age group. The buccal mucosa and commissures are most frequently involved, followed in descending order by the alveolar mucosa, tongue, lip, hard and soft palate, floor of the mouth and gingiva. The histological picture in leukoplakia is quite variable.[2]

Axell et al classified leukoplakia into homogeneous (which carries the lowest risk of malignant potential) and non-homogeneous which is of three types: erosive, nodular or speckled and verrucosa (carries the highest risk of malignant potential).[3]

Pindborg et al, during a study of 248 patients with oral leukoplakic lesions found that 4.4% of the lesions underwent a malignant transformation.[2] Mehta et al, in a survey of 50,915 Indian patients found that the incidence of leukoplakia was up to 4.0%. They further elaborated that epithelial atypia was observed in 8.4% of homogeneous leukoplakia and in 59.1% of speckled leukoplakia.[4]

Oral submucous fibrosis (OSMF) is a chronic disease of the oral cavity, which is characterized by an epithelial and subepithelial inflammatory reaction followed by fibroelastic changes in the submucosa.[5] An exclusive feature is the formation of firm, vertical fibrous bands, located in the oral mucosa, which ultimately lead to severe restriction of movement of mouth, including the tongue, thus causing difficulty in opening the mouth, eating, swallowing, and phonation. This disease occurs most commonly in South-East Asia but cases have been reported worldwide in countries like Kenya, China, UK, Saudi Arabia and other parts of the world.[6] Tilakaratne et al reported that areca nut is the main etiological

factor for OSMF.[7] Excessive use of areca nut may cause fibrosis due to increased synthesis of collagen and induce the production of free radicals and reactive oxygen species, which are responsible for high rate of oxidation/peroxidation of polyunsaturated fatty acids which affect essential constituents of cell membrane and might be involved in tumorigenesis.[8,9]

Biochemical studies in evaluation of cancer have shown that various substances alter quantitatively in the serum during tumor development and are referred to as tumor markers.[10] So, if the biochemical changes occur even before frank cancer has occurred, we can predict even in oral precancerous lesions and conditions whether a particular individual with the underlying biochemical defect would develop cancer or not at a later date.

Lipids are major cell membrane components essential for various biological functions including cell growth and division of normal and malignant tissues. They are homogeneous group of compounds related more by physical than chemical properties. An alteration in the circulatory cholesterol levels has been found to be associated in the etiology of breast cancer and colorectal cancer.[11] However, only a few reports are available on plasma lipid profile in head and neck lesions.[12] This study was undertaken to evaluate the role of serum lipids as tumor markers in the diagnosis of oral precancerous lesions and conditions. It can be suggested that Serum lipid status may be considered as a useful indicator for initial changes occurring in the neoplastic cells.

MATERIALS AND METHODS

A hospital-based study was conducted in 25 clinically diagnosed and histopathologically proven patients of Oral Potentially malignant disorders namely Oral Leukoplakia and Oral Submucous fibrosis attending the outpatient department of Oral Medicine and Radiology, Ragas Dental College and Hospital, Chennai after the institutional ethical committee clearance. Written consent was taken from the patients for the same. All the patients underwent recording of signs, symptoms, and detailed history including habits, histopathology, and extended lipid profile estimation. Twenty five healthy individuals, matched for age and sex, who had no complaint or any other major illness in recent past, were included as controls. The patients were also compared with 25 persons diagnosed with oral squamous cell carcinoma

a. Normal controls-Group-I : 25

b. Patients with Oral Potentially malignant disorders-Group-II : 25

c. Patients with Oral Squamous cell carcinoma–Group-III:

Fasting blood samples were collected in plain vials. Serum was collected after centrifugation and stored at –80°C until analyzed. Serum levels of Total cholesterol (TC), High density lipoprotein cholesterol (HDL), Low density lipoprotein cholesterol (LDL), Very low density lipoprotein cholesterol (VLDL), and Triglyceride (TGL) were calculated by using Autospan Reagents (Hitech Diagnostics, India). Statistical analysis was performed utilizing SPSS package.

RESULTS

The following parameters which constitute serum lipid profile, were studied in all the groups: Cholesterol, HDL, LDL, VLDL, TGL.

Table 1 shows general information of number of subjects, age and sex wise distribution in all the three groups. The study included 25 controls in Group I, 25 Oral Potentially malignant disorders patients in Group II and Oral Squamous cell carcinoma patients in Group III .The age range was from 23 to 63 years with mean age of 39.08 for Group I, the age range was 22 to 58 years with mean age of 37.4 for Group II, and the age range was from 46 to 70 years with mean age of 59.08 for Group III. There is a clear male predilection of 23(92%) and 16(64%) compared to the females who accounted for 2(8%) and 9(36%) in Group II and Group III respectively.

Table -1: Showing Number of Subjects, Age And Sex Wise Distribution In All Three Groups.

No of subjects		**Groupi**	**Group ii**	**Groupiii**
		25	**25**	**25**
Age(years)	Mean	39.08	37.4	59.08
Sex	Male	17	23	16
	Female	8	2	9

Table 2 All the 5 parameters of serum lipid profile were compared for both controls and diseases groups (Table-2). Mean and SD were calculated. In control group lipid profile parameters were, TC with mean and SD of 172.56 ± 29.2 , HDL cholesterol with mean and SD of 42.7 ± 3.1, LDL cholesterol with mean and SD of 102.6 ± 24.4, TGL with mean and SD of 151 ± 20.6 and VLDL cholesterol with mean and SD of 33.± 9.4. In Group II, lipid profile parameter were, TC with mean and SD of 159.84±15.5, HDL cholesterol with mean and SD of 40.72±3.2, LDL cholesterol with mean and SD of 91.16±17.0, TGL with mean and

SD of 141.04±53.4, VLDL cholesterol with mean and SD of 29.96±10.7. In Group III, lipid profile parameter were, TC with mean and SD of 157.56±12.3, HDL cholesterol with mean and SD of 38.92±2.5, LDL cholesterol with mean and SD of 92.44±14.6, TGL with mean and SD of 131.16±44.7., VLDL cholesterol with mean and SD of 26±9.

Table -2 Showing Serum Lipid Profile In All Three Groups.

Groups	Number of subjects	TC Mg%	LDL Mg%	HDL Mg%	VLDL Mg%	TGL Mg%
I	25	172.56±290.2	102.60±240.2	42.76± 3.1	33.32± 9.4	151.68±20.5
II	25	159.84±150.5	91.16± 17.0	40.72± 3.2	27.96± 10.7	141.04±53.4
III	25	157.44±120.3	92.44± 14.6	38.92± 2.5	26.00± 26.9	131.16±44.7
ANOVA	F P	3.84 0.01	2.26 0.07	5.70 0.001	3.75 0.01	1.50 0.22

TABLE 3 : when comparing Group 1 & 2, statistically significant difference were noticed for TC, HDL ($p < 0.05$), while for LDL,TGL and VLDL it was statistically non significant ($p >0.05$).

When comparing Group 1 & 3, statistically significant difference were noticed for TC, HDL, and VLDL ($p < 0.05$),while for TGL and LDL it was statistically non significant ($p >0.05$).

Table 3: Showing Comparison of Serum Lipid Parameters Among All Three Groups.

		TC	LDL	HDL	VLDL	TGL
GROUP1&2	Mean Difference P Value	12.60 **<0.01**	11.44 0.91	1.04 **<0.05**	5.36 0.13	10.64 0.64
GROUP1&3	Mean Difference P Value	14.8 **<0.01**	10.13 0.15	2.84 **<0.001**	7.32 **<0.05**	20.52 0.19
GROUP2&3	Mean Difference P Value	2.28 0.91	1.28 0.97	1.80 0.09	1.96 0.75	9.88 0.68

DISCUSSION

Head and neck cancer is one of the leading causes of morbidity and mortality and habit of tobacco consumption is a known etiological factor for development of oral precancerous disease and head and neck cancer. Patients with oral precancerous conditions have also been reported to show a significant tendency to develop cancer. Cholesterol is an amphipathic lipid and as such, is an essential structural component of all cell membranes and of the outer layer of plasma lipoproteins.

Regulation of cholesterol is mediated by lipoprotein receptors. Plasma triglycerides and cholesterol are packed into lipoproteins for transport. Cholesterol is an essential constituent

of lipoprotein fractions like LDL, HDL and VLDL. In some malignancies, serum cholesterol undergoes early and significant changes. Low levels of cholesterol in the proliferating tissues and in blood compartments could be due to the rapidly dividing cells in malignancies. The habit of tobacco consumption is a known etiological factor for development of oral precancerous disease and head and neck cancer. Patients with oral precancerous conditions have also been reported to show a significant tendency to develop cancer. It is believed that tobacco carcinogens and excessive use of areca nut induce generation of free radicals and reactive oxygen species, which are responsible for high rate of oxidation / peroxidation of polyunsaturated fatty acids. Because of lipid peroxidation there is greater utilization of lipids including total cholesterol, lipoproteins and triglycerides for new membrane biogenesis. Cells fulfill these requirements either from circulation, by synthesis through metabolism or from degradation of major lipoprotein fractions like VLDL, LDL, and HDL.[12] Hence the present study was done to validate Serum lipid changes as biological marker for Oral Potentially malignant disorders and Oral squamous cell carcinoma.

The Studies by Patel et al. showed a significant decrease in plasma TC and HDL cholesterol in both patients with cancer and oral precancerous conditions. Their study also showed lower levels of VLDL cholesterol and TGL in cancer as well as in patients with oral precancerous conditions as compared to controls.[12] In our study, there was a significant decrease in levels of serum TC, HDL which were observed in patients with Potentially Malignant Disorders and There was a significant decrease in the serum TC, HDL, VLDL in patients with oral carcinoma.

This is also consistent with another study conducted by **Lohe et al**[13] which showed a significant decrease in plasma TC,HDL,VLDL in patients with cancer and oral precancerous conditions. With p value of $P<0.001$ when compared with controls. It was postulated that low levels of cholesterol in the proliferating tissues and in blood compartments could be due to the process of carcinogenesis. It was postulated that low HDL is an additional predictor of cancer and it might be a consequence of disease that is mediated by utilization of cholesterol for membrane biogenesis.

The present study found a significant reduced VLDL when OSCC group was compared with control group with p value <0.05. But there was no significant difference in VLDL when PMD group was compared with controls. It is believed that tobacco carcinogens induce lipid peroxidation in which 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. The present study could not find a significant result in LDL and TGL when both the groups were compared with control group with p value0.07. This is consistent with study conducted by Lohe et al.[13] This is also in consistent with study by Chawda et al[14] who didnot find a significant decrease in LDL.

CONCLUSION

To conclude an inverse relationship exists between serum lipid profile in Oral cancer and Oral Potentially Malignant disorders. The lower serum lipid status may be a useful indicator for initial changes occurring in neoplastic cells. Variability of the values of serum lipid profile in precancerous condition and cancer patients may be due to multiple reasons, such as age, nutritional status, body mass index, alcohol consumption, exercise habits. The variability in levels of the 5 parameters of lipid profile might also arise from methodological difference. The present findings are drawn by a smaller sample size but the findings strongly warrant an indepth study on a large sample size of oral cancer. Further study with larger sample size and additionally a long term follow up of PMD subjects with periodic estimation of lipid profile would be needed to establish correlation between a trans formation from precancerous state to malignancy. Thus lipid profile may be used as a marker for malignant transformation in PMD and hence early detection of malignancy would give way to early treatment thereby increasing the survival rate in these patients.

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