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Alterations of serum lipid profile in oral submucous fibrosis

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ABSTRACT

Background: Oral cancer is one of the most common form of malignancies in India. In many cases it develops at the site of premalignant lesion. Of all oral premalignant conditions, oral submucous fibrosis (OSMF) is of greater concern because of its disabling nature and relative greater chances of malignant transformation. This study is aimed to evaluate the serum lipid profile in OSMF patients as the change in lipid levels may have a diagnostic and prognostic role in the potentially malignant lesions. The present study aimed to evaluate the alteration in serum lipid profile in OSMF and to compare them with healthy controls and to correlate the relationship between pathogenesis of OSMF and lipid profile.
Methods: It is a case control study. The study included 50 diagnosed cases of OSMF and 50 matched healthy controls. Fasting venous blood of 3 ml was collected in both cases and controls and serum was separate. Fasting serum lipid profile including total cholesterol (TC), very low density lipoproteins (VLDL), low density lipoproteins (LDL), high density lipoproteins (HDL) and triglycerides (TG) were measured using automatic analyser. Statistical analysis was done using student 't' test .Pearson's correlation was performed to establish the relationship between study variables.
Results: It was observed that there was statistically significant decrease in serum total cholesterol, TG, LDL, VLDL and HDL observed in patients with OSMF as compared to the control group ($p<0.005$).
Conclusions: The low lipid levels associated with OSMF indicates that there is inverse relationship between oral cancer and serum lipid profile. Decrease in the lipid levels may be considered as a valuable biochemical marker in the early diagnosis and prognosis of oral malignancy.

Keywords: OSMF, TC, HDL, VLDL, Premalignant, Oral cancer, Biochemical marker

INTRODUCTION

Oral submucous fibrosis (OSMF) is a chronic, debilitating disease characterised by juxtaepithelial fibrosis of the oral cavity.[1] It is a precancerous condition- a generalized pathological state of the oral mucosa associated with a significantly increased risk of cancer according to world health organization (WHO). [2] Although occasionally preceded by, or associated with, formation of vesicles, it is always associated with a juxtaepithelial inflammatory reaction followed by fibro elastic change of the lamina propria and epithelial atrophy that leads to stiffness of the oral mucosa and causes trismus and an inability to eat.[3]

Oral submucous fibrosis can be seen at any age except for young children. The predominant age group affected is 20-40 years. Compared to traditional betel quid, gutkha chewing tends to begin at a younger age and has a shorter time to the development of disease, so cases of oral submucous fibrosis have been seen as young as 11 years of age.

The pathogenesis of the disease is not well established, but the cause of OSMF is believed to be multifactorial.

Factors include areca nut chewing, ingestion of chillies, genetic and immunologic processes, nutritional deficiencies, and other factors. Iron deficiency anemia, vitamin B complex deficiency, and malnutrition are promoting factors that derange the repair of the inflamed oral mucosa, leading to defective healing and resultant scarring.[4]

Betel quid chewing is seen almost exclusively in the Indian subcontinent, South East Asia and western Pacific. Tilakaratne et al reported that areca nut is the main etiological factor for OSMF.[5] 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 may involve in tumorogenesis.[6-8] Because of the lipid peroxidation, there is a greater utilization of lipids 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, LDL or HDL. Studies by various researchers have reported association of serum/serum lipids and lipoproteins with different cancers, as cholesterol is essential for maintenance of structural and functional integrity of all biological membranes.

The present study was planned to evaluate the serum lipid profile in OSMF patients as the change in lipid levels may have a diagnostic and prognostic role in the potentially malignant lesions.

METHODS

This was a case control study. The study was carried out on 50 cases of clinically diagnosed OSMF in the age group 20-50 years attending the otorhinolaryngology (ENT) outpatient department of Koppal Institute of Medical Sciences (KIMS), Koppal. Fifty (50) age and sex matched healthy subjects were taken as controls. The study was conducted over a period of one and half year from June 2015 to December 2016. Ethical clearance was obtained from the institute's ethical clearance committee. Informed consent was taken from the cases and controls after explaining the procedure. The 50 OSMF patients were clinically examined and diagnosed. Later they were confirmed histopathologically following punch biopsy.

Exclusion criteria

- Subjects not willing to participate in the study
- Patients on chemotherapy or radiotherapy or undergoing any surgery for OSMF
- Those with diabetes ,hypertension ,obesity , hepatic disease, malabsorption syndromes
- Those with overt thyroid dysfunction ,chronic kidney disease ,chronic liver disease, those are on corticosteroid therapy, those are on lipid lowering agents
- Patients with h/o myocardial infarction in recent past (2weeks)

Biochemical analysis

A fasting blood sample of 3 ml venous blood was collected under aseptic precautions in a plain vial. It was allowed to clot and serum was separated by centrifugation. Lipid profile was analysed using automated analyser by following methods

- Triglycerides by enzymatic method using Glycerol-3-phosphate as substrate
- Total cholesterol by Cholesterol oxidase-peroxidase method.
- HDL cholesterol by Precipitation (with phosphotungstic acid) method.
- LDL cholesterol using Friedwald formula.

$$LDL = TC–(HDL+TG/5)$$

Statistical analysis

Data was expressed in terms of mean±SD. Chi- square test was applied to estimate the difference between the two groups of population. Unpaired 't'-test was used to study the changes in serum lipid levels between the study groups. Pearson correlation was performed to establish the relationship between study variables. P value <0.05 was considered statistically significant.

RESULTS

This was a comparative case control study conducted on 50 cases of OSMF (n=50) and 50 age and sex matched healthy controls (n=50). Serum lipid levels were estimated and analyzed in cases and controls. The results were expressed as mean±standard deviation.

Table 1: Age distribution of cases and controls.

	Cases- OSMF	Controls	P value
Mean age (years)	45.5±11.7	45.2±10.3	>0.05, not significant

The age distribution of cases and controls is depicted in Table 1. The mean age (in years) of cases was 45.5±11.7 years and that of controls was 45.2 ±10.3 years and was not significant (p>0.05).

Table 2 shows the gender distribution. Out of 50 cases of OSMF, 30 (60%) were males and 20 (40%) were females. Out of 50 controls, 30 (60 %) were males and 20 (40%) were females and it was not statistically significant

(p=0.38). In general, males were more commonly affected than females .The incidence of OSMF was most common seen between 2nd and 4th decade.

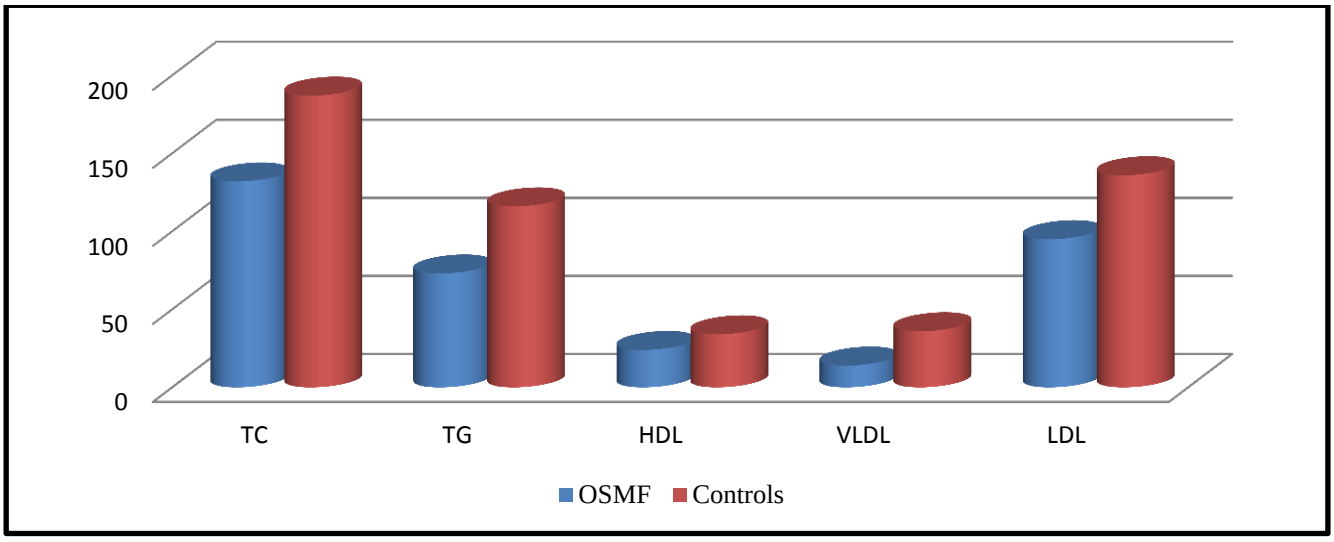
The mean serum Cholesterol, serum HDL, serum LDL, serum VLDL and serum TG levels in OSMF cases and control group are shown in Table 3. A statistically significant reduction (P<0.001) was noted between the control group and OSMF cases for all lipid parameters. (Figure 1).

Table 2: Gender distribution of cases and controls.

Gender	Cases- OSMF-n (%)	Controls- n (%)
Male	30 (60)	30 (60)
Female	20 (40)	20 (40)

Table 3: Comparison of serum lipid levels between controls and OSMF.

Parameters	Cases- OSMF	Controls	Normal values	P value
TC	132.95±43.03	184.23±19.47	150-200	0.504
HDL	24.41±6.72	34.52±3.47	35	0.833
LDL	95.41±38.36	86.55±20.33	150	0.112
VLDL	14.62±3.01	36.17±10.44	15-40	0.171
TG	73.09±15.01	116.25±29.40	150	0.302



TC- total cholesterol, TG- triglyceride, HDL- high density lipoprotein, VLDL- very low density lipoprotein, LDL- low density lipoprotein

Figure 1: Comparison of the mean values of serum lipids in between OSMF cases and healthy controls.

DISCUSSION

Lipids are major cell membrane components essential for various biological functions including cell growth and division of normal and malignant tissues. The changes in lipid profile have long been associated with cancerous and precancerous conditions because lipids play a key role in maintenance of cell integrity.[9] As lipids may play a role in precancer and cancer, this study was aimed to estimate serum lipid profile in oral submucous fibrosis groups and to compare the values with those values from control groups.

The habit of tobacco consumption is a known etiologic factor for development of oral precancerous diseases and head/neck cancer.[10,11] Cholesterol which is an amphi-pathic 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-esterin tissues and in serum lipoprotein. It is synthesized from acetylCoA in many tissues and is ultimately eliminated as cholesterol or bile salts from the body. In the circulation, lipoprotein transports free cholesterol and it readily equilibrates cholesterol in other lipoproteins and in membranes.[12-15] Free radicals and reactive oxygen species are generated from tobacco carcinogens which are responsible for high rate of oxidation/peroxidation of polyunsaturated fatty acids. It results in greater utilization of lipids including total cholesterol, lipoproteins and triglycerides for new membrane biogenesis. Cells fulfil these requirements either from circulation, or by synthesis through metabolism or from degradation of major lipoprotein fractions like VLDL, LDL, and HDL. Earlier studies have shown alteration of serum lipid profiles in head and neck and other cancers.[13-15] In the

present study, a significant decrease in serum total cholesterol, HDL, LDL, VLDL and TG was observed in oral SCC patients as compared to the controls.

The results in our study add to the evidence of an inverse relationship between serum lipid profile and oral submucous fibrosis. The decrease in total cholesterol in patients with OSMF could be due to the excessive use of areca nut and also due to rapidly dividing cells in malignancy. In areca nut the major alkaloid arecoline undergoes nitrosation and gives rise to N- nitrosamine, which might have cytotoxic effect on the cells. This leads to lipid peroxidation by reactive free radicals generation and also leads to greater utilization of lipids as explained above.[16,17]

In our study, the decrease in total cholesterol levels may be a useful indicator reflecting initial changes occurring in precancerous and neoplastic conditions. The evidence suggests that in precancerous conditions like OSMF cells are able to remetabolize lipids for their growth and to generate phospholipids membranes. Recent progress in molecular biology will assist researchers in the near future to identify the genes and enzymes of lipid metabolic pathways.

CONCLUSION

Our study shows that there is an inverse relationship between serum lipid profile and OSMF. The change in serum lipid levels may be used as a diagnostic or prognostic biochemical indicator for early diagnosis of oral premalignant and malignant conditions. However, a detailed study on large sample size and on role of cholesterol in neoplasia should be carried out for better understanding of this inverse relationship of serum lipid profiles and oral pre malignant and malignant conditions

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