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Original Article

Alteration in plasma lipid profile in precancerous conditions

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Abstract

Objective: Carcinoma is an uncontrolled multiplication of cells, such cell production requires to replace lost cells, that will place a strain on all normal processes and deplete normal stores, one very important component for every cell is the lipid used in its cell wall. This large scale unplanned cell production would deplete cholesterol stores and possibly manifest as a fall of lipid values. Hence the present study was carried out to evaluate changes in plasma lipid profile in patients with oral precancerous conditions and to evaluate if any relation exists between the plasma lipid level and malignant potential.

Methods: A total sample size of 56 subjects was chosen, with the study group consisting of a total of 28 patients 14 with OFS and 14 with LP. The control group consisted of 28 sex and age matched individuals, with out any systemic or oral condition. The histopathological confirmation was done and the patients were recalled with a minimum of 12 hour of fasting for blood examination for complete lipid profile.

Results: The present study showed that 3 parameters (TC, HDL, LDL) of lipid profile were reduced in Oral Precancerous cases as compared to age and sex matched healthy controls.

Statistical Analysis: Mean and Standard Deviation (SD) was calculated for each group. One way ANOVA was used for multiple group comparison and student's t test (unpaired) for group wise comparison. Diagnostic validity tests were performed using lipid values as biomarkers to differentiate different disease groups with healthy controls. For all the tests p value of 0.05 or less was used for statistical significance

Conclusion: The estimation of lipid profile can be considered as a good marker for increased cell turnover. However this will also have to be confirmed by using a larger sample size.

Key words: Precancer, Carcinoma, Cholesterol, Lipid.

Introduction

Premalignancy / precancer can be defined as any lesion that displays the metabolic and histologic activity found in cancerous lesions and with in whose boundaries it is possible, but not mandatory, for a carcinoma to develop. Many factors modify the possibility and rapidity of transformation such as immunologic status of the host (modified by disease/therapy), precancerous activity, and high risk sites (lower lip, vermillion border of tongue, floor of the mouth)[1].

A variety of premalignant conditions (PMC) including Sideropenic dysphagia, Lichen planus (LP), Oral submucous fibrosis (OSF), Syphilis, Discoid lupus erythematosus (DLE), Xeroderma pigmentosum, Epidermolysis bullosa (EB) affect oral mucosa[2], However, the most common premalignant conditions of the oral cavity include oral submucous fibrosis and lichen planus**.** Frequency of malignant development is 7 – 12% in OSF[3] and 0.4 – 12.3% in LP patients[4].

Fundamentally the development of a malignancy requires the uncontrolled and excessive proliferation of cells. These newly forming cells would need many basic components well above the normal limits, used in physiological process. One such component is lipids which form major cell membrane components essential for various biological functions including cell division and growth of normal and malignant tissues. The increased requirement of lipids to fulfill the need of these new cells would be expected to diminish the lipid stores. Variation

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in blood cholesterol levels in diagnosis and treatment of various diseases has been studied. Cancer patients as a group demonstrated significantly lower total, esterified cholesterol and low density lipoprotein (LDL) cholesterol, compared with non cancer patients. However, only a few reports are available on plasma lipid profile in head and neck cancers[5].

Therefore the present study was carried out to evaluate changes in plasma lipid profile of patients with precancerous conditions and to examine if any relation exists between the changes and increasing malignant potential.

Methodology

A total sample size of 56 subjects was chosen, with the study group consisting of a total of 28 patients, 14 with OSF and 14 with LP. The control group consisted of 28 sex and age matched individuals, with out any systemic or oral condition.

Controls and Cases were divided into 2 groups:
Group 1 – Controls
Group 2 – Cases

Group 2 was again subdivided into:

- 2a – OSF
- 2b – LP

The features considered for histopathological confirmation of OSF[3] were epithelial hyperplasia in early and epithelial atrophy in advanced stages, juxta epithelial hyalinization of collagen fibers and combination of dilated and constricted blood vessels.

For LP[3] the features considered were hyperparakeratosis or hyperorthokeratosis, acanthosis, development of saw tooth appearance of the rete pegs, band like subepithelial infiltrate consisting of T cells and histiocytes and degenerating basal keratinocytes.

Method

Detailed clinical history of oral precancerous condition individuals was recorded. After getting informed consent, biopsy of the patients with suspected oral precancerous conditions was obtained and subjected to histopathological examination. After the histopathological confirmation was done, the patients were recalled with a minimum of 12 hour of fasting for blood examination for complete lipid profile. 5 ml of fasting blood was collected from a large peripheral vein from selected subjects and put into EDTA containing test tubes. Samples were centrifuged for 5 minutes at 3000 revolution per minute (rpm); plasma was collected and stored in refrigerator until analyzed. Samples were analyzed using the kit Accurex (Biomedical private limited) as per the instructions provided by the manufacturer, using a semi-autoanalyser.

Complete lipid profile was checked in each case, which comprised of Total cholesterol (TC), Triglycerides (TG), High density lipoprotein (HDL) cholesterol, Low density lipoprotein (LDL) cholesterol, Very Low density lipoprotein (VLDL) cholesterol

Mean and Standard Deviation (SD) was calculated for each group. One way ANOVA was used for multiple group comparison and student's t test (unpaired) for group wise comparison. Diagnostic validity tests were performed using lipid values as biomarkers to differentiate different disease groups with healthy controls. For all the tests p value of 0.05 or less was used for statistical significance.

Results

The following parameters which constitute plasma lipid profile, were studied in both the groups: Total cholesterol (TC), High density lipoprotein cholesterol (HDL), Low density lipoprotein cholesterol (LDL), Very low density lipoprotein cholesterol (VLDL), and Triglyceride (TG)

Table 1 shows general information of number of subjects, age and sex wise distribution in both groups. The study included 28 controls and cases with a mean age and standard deviation of 28.0 ± 7.5 controls and 31.4 ± 10.5 for cases. The age range was 19 – 46 yrs for controls and 17 – 50 yrs for cases.

All the 5 parameters of plasma lipid profile were compared for both controls and cases (Table-2). Mean and SD was calculated**.** In control group lipid profile parameters were, TC with mean and SD of 171.3 ± 16.4 and ranging between 140.0 – 215.6 mg/dl, HDL cholesterol with mean and SD of 40.9 ± 8.3 and ranging between 29.0 – 59.0 mg/dl, LDL cholesterol with mean and SD of 108.7 ± 19.4 and ranging between 74.5 – 157.5 mg/dl, TG with mean and SD of 115.3 ± 16.1 and ranging between 90.0 – 148.0 mg/dl and VLDL cholesterol with mean and SD of 23.± 3.2 and ranging between 18.0 – 29.6 mg/dl. (Graph 1-5). In study group lipid profile parameter were, TC with mean and SD of 146.8±11.0 and ranging between 128.4-165.0 mg/dl, HDL cholesterol with mean and SD of 29.9±4.6 and ranging between 21.3-39.6 mg/dl, LDL cholesterol with mean and SD of 93.6±11.8 and ranging between 68.4-115.0, TG with mean and SD of 117.0±21.2 and ranging between 69.7-157.0 mg/dl, VLDL cholesterol with mean and SD of 23.4±4.3 and ranging between 13.9-31.4 mg/dl.

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

Comparison of controls and subjects(OSF and LP) for TC, HDL, LDL, TG and VLDL showed controls with mean and SD of 171.3± 16.4, 40.9± 8.3, 108.7±19.4, 115.3±16.1, & 23.1±3.2, OSF with mean and SD of 150.1±8.9, 30.2±3.8, 94.9±8.5, 125.2±16.6, & 25.0±3.3, and LP with mean & SD of 143.6±12.2, 29.7±5.3, 92.2±14.5, 108.8±22.7 & 21.8±4.5 for TC, HDL, LDL, TG and VLDL respectively. The results were statistically significant for TC, HDL, LDL, TG and VLDL ($p<0.05$) (Table-4).

When lipid parameter were compared between Controls & OSF, it showed statistically significant values ($p<0.05$) for TC, HDL & LDL while TG & VLDL were statistically non significant ($p<0.08$) in OSF cases. Similar results were seen between Controls & LP, but when lipid parameter were compared between OSF & LP, TG & VLDL were statistically significant ($p<0.05$), while TC, HDL & LDL were statistically non significant ($p<0.12$, $p<0.74$ & $p<0.54$ respectively) (Table 5).

Table 1: Sample size, age & sex wise distribution of controls & cases

No of subjects		**Control**	**Cases**
		28	**28**
Age(years)	Mean ± SD Range	28.0 ± 7.5 19 – 46	31.4 ± 10.5 17 – 50
Sex	Male	16	16
	Female	12	12

Table 2: Mean, SD and range values of lipid profile in cases and controls

Groups	**No of subjects**		**TC**	**HDL**	**LDL**	**TG**	**VLDL**
Controls	28	Mean± SD	171.3± 16.4	40.9± 8.3	108.7±19.4	115.3±16.1	23.1±3.2
		Range	140.0-215.6	29.0-59.0	74.5-157.5	90.0-148.0	18.0-29.6
Cases	28	Mean± SD	146.8±11.0	29.9±4.6	93.6±11.8	117.0±21.2	23.4±4.3
		Range	128.4-165.0	21.3-39.6	68.4-115.0	69.7-157.0	13.9-31.4

Table 3: Mean difference, t value and p value of Controls and Cases

	TC	**HDL**	**LDL**	**TG**	**VLDL**
Mean difference	24.5	11.0	15.1	1.7	0.3
t value	6.29	5.80	3.39	0.33	0.33
p value	< 0.001, S	<0.001, S	<0.01, S	0.74, NS	0.74, NS

Table 4: Inference between Controls and Cases

	No	**TC**	**HDL**	**LDL**	**TG**	**VLDL**
1. Controls	28	171.3± 16.4	40.9± 8.3	108.7±19.4	115.3±16.1	23.1±3.2
2a. OSF	14	150.1±8.9	30.2±3.8	94.9±8.5	125.2±16.6	25.0±3.3
2b. LP	14	143.6±12.2	29.7±5.3	92.2±14.5	108.8±22.7	21.8±4.5
ANOVA	F	21.7	17.8	6.1	3.04	3.05
	P	< 0.001	<0.001	<0.05	<0.05	<0.05

Table 5: Inter group inference between groups

		TC	**HDL**	**LDL**	**TG**	**VLDL**
1 – 2a	**T**	4.46	4.51	2.52	1.83	1.82
	p	<0.001, S	< 0.001, S	< 0.05, S	0.08, NS	0.08, NS
1 – 2b	**T**	5.50	4.54	2.78	1.04	1.05
	p	< 0.001, S	<0.001, S	< 0.05, S	0.08, NS	0.03. NS
2a – 2b	**T**	1.61	0.33	0.61	2.18	2.18
	p	0.12, NS	0.74, NS	0.54, NS	<0.05, S	<0.05, S

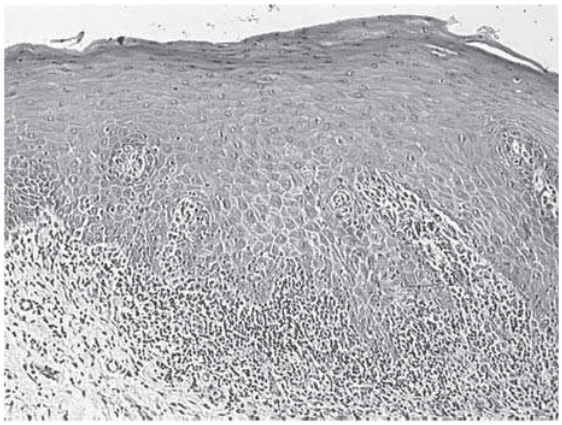


Fig 1: Histopathological picture of lichen planus

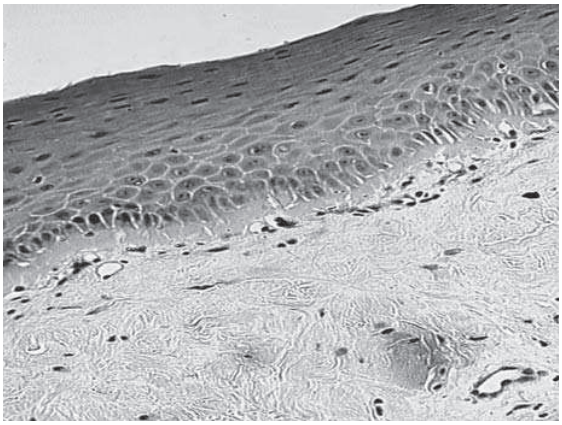
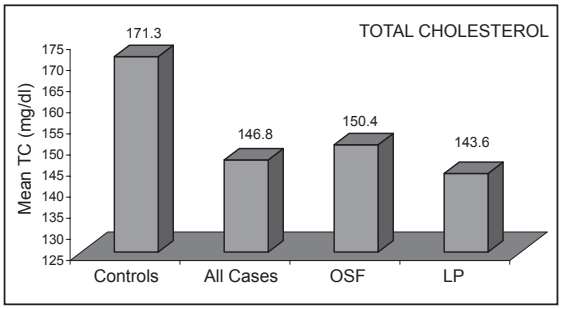
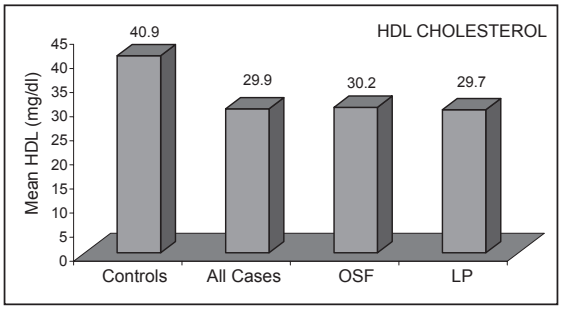


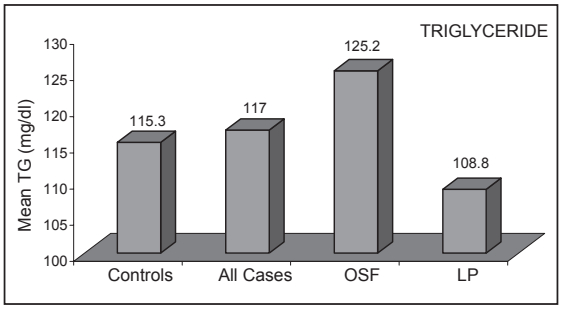
Fig 2: Histopathological picture of oral sub mucous fibrosis



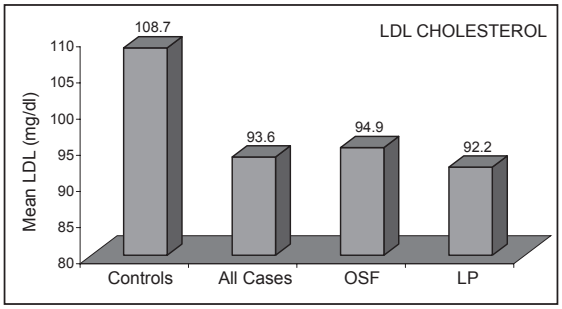
Graph 1: Total cholesterol in controls, cases.



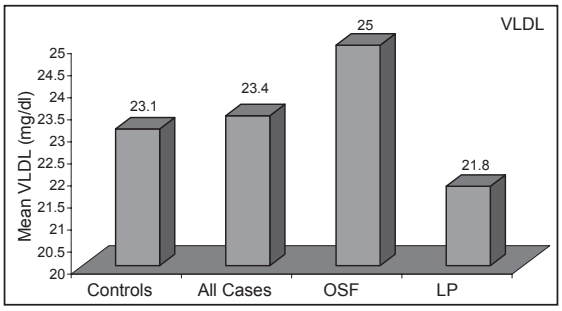
Graph 2: HDL cholesterol in controls, cases.



Graph 3: Triglyceride in controls, cases.



Graph 4: LDL in controls, cases.



Graph 5: VLDL in controls, cases.

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. It is believed that tobacco carcinogens induce generation of free radicals and reactive oxygen species, which are responsible for high rate of oxidation / per oxidation of polyunsaturated fatty acids. Because of lipid per oxidation 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[5]. Hence the present study was done to determine the alteration in plasma lipid profile in precancerous condition patients.

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 TG in cancer as well as in patients with oral precancerous conditions as compared to controls. In our study there was no statistical difference in the levels of TG and VLDL in both cases and controls. In their study plasma LDL cholesterol levels did not reveal any significant difference among cancer and oral precancerous condition patients, where as in our study significant decrease in oral precancerous condition patients was seen as compared to controls[5].

Studies by C. G Alexopolous found that there is significantly lower value of TC and LDL cholesterol in men with cancer (lung cancer and hematological cancer) as compared to controls. These results were similar to our study performed on precancerous condition patients. Their study also found values of TG levels was not statistically significant for cancer men and controls, similar to our study[6].

Some of the previous studies stated that serum cholesterol levels were inversely associated with incidence of cancer[7,8,9,10]. Our study performed on precancerous condition also showed inverse relation between plasma cholesterol levels and precancerous condition, these changed levels might indicate the progression of these lesions towards malignancy.

Study by Jacqueline M Halton found a significant reduction in values of HDL in acute leukemic patients. However the author also found out elevated TG levels, our study on oral precancerous patients also showed significant reduction in values of HDL levels[11].

The results of 5 parameters (TC, HDL, LDL, VLDL, TG) of lipid profile tested in our study are in agreement with above mentioned studies done on cancer patients (lung cancer, hematologic cancer, breast cancer), however there are differences between the studies when various parameters are considered individually.

Variability of the values of plasma 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.

A larger study sample and long term follow up of cases with periodic estimation of lipid profile would be needed to establish correlation between a transformation from a precancerous state to malignancy.

Conclusion

The present study showed that 3 parameters (TC, HDL, LDL) of lipid profile were reduced in OPC cases as compared to age and sex matched healthy controls. Reduced lipid values in plasma may be due to greater utilization of lipids for new membrane biogenesis.

Further study with larger sample size and additionally a long term follow up of these OPC cases with periodic estimation of lipid profile would be needed to establish correlation between a transformation from precancerous state to malignancy.

Some values were lower in LP patients in comparison with OSF patients. The estimation of lipid profile can be considered as a good marker for increased cell turnover. However this will also have to be confirmed by using a larger sample size.

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