

Original Research

Evaluation of Serum Lipid Profile in Head and Neck Cancer, OSMF and Leukopkia Patients

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ABSTRACT

Background:

The lipids are important ingredients of cell membranes and play a vital role in numerous biological processes, including maintaining the integrity of the cell. **Materials & Methods:** In the perspective of this view, influences on levels of various serum lipid profile parameters, namely, Total cholesterol (TC), LDL cholesterol, VLDL cholesterol, HDL cholesterol, Triglycerides (Trg) have been discussed with an aim to correlate & evaluate plasma lipid profile in head & neck cancer, oral submucous fibrosis, leukoplakia and normal control group. **Result:** The lower plasma lipid status may be a useful indicator for initial changes occurring in neoplastic cells. Plasma TC, HDL, LDL and TG values were lower in squamous cell carcinoma. OSMF and leukoplakia patients than healthy individuals. The most reduced levels are present in cancer patients while OSMF and Leukoplakia patients have similar levels. There was statistically significant difference present in lipid profile of OSMF, leukoplakia and squamous cell carcinoma patients than in normal groups. There was no statistically significant difference present between lipid profile of OSMF and leukoplakia patients. Lipid profile of squamous cell carcinoma was lower than OSMF patients. Lipid profile of squamous cell carcinoma was lower than leukoplakia patients. **Conclusion:** Plasma lipid profile levels may be a useful indicator reflecting initial changes occurring in pre-cancerous and neoplastic conditions. The lower plasma lipid status may be useful bio-marker indicator for initial change occurring in neoplastic cells.

Key words: High density lipid, Lipid profile parameters, Low density lipid, Cholesterol.

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INTRODUCTION

Lipids (Greek : Lipos fat) may be regarded as organic substance which are relatively insoluble in water and soluble in organic solvent (alcohol ether etc.) Potentially related to fatty acids and are utilized by the living cell. Lipids are broadly:

Lipoproteins - Lipoproteins are molecular complexes of lipids with proteins. They are the transport vehicles for lipids in the circulation. There are five types of lipoproteins, namely chylomicrons, very low density lipoproteins (VLDL), Low density lipoproteins (LDL), high density density Lipoproteins (HDL) and free fatty acid -albumin complexes¹. The main function of

phospholipids in mammalian cells is to maintain the structure of cellular membranes. Changes in lipid profile of membranes alter fluidity, which in turn affects permeability of membranes. Alterations in membrane lipid levels can also influence cell proliferation and viability. Phospholipids are well known for their amphiphilic nature and are surface active².

Neutral lipids are uncharged. Ex. - mono, di, and triacylglycerols, cholesterol and cholesteric Esters¹.

Cholesterol - Cholesterol (Greek : Chole -bile) was first isolated from bile. Cholesterol literally means " solid alcohol bile". It is an amphipatic lipid, soluble in organic solvent such as chloroform, benzene, ether etc. It is an

essential structural component of all the cell membranes and of the outer layer of plasma lipoproteins. It is widely distributed in all the cells of the body. It is present in tissues and in plasma lipoprotein either as free cholesterol or combined with a long-chain fatty acid, as cholesterol ester. It is synthesized in many tissues from acetyl-CoA and is ultimately eliminated from the body in the bile as cholesterol or bile salts. Lipoprotein transports free cholesterol in the circulation, where it readily equilibrates cholesterol in other lipoproteins and in membranes³.

Cholesterol ester is a stored form of cholesterol found in most tissues. It is transported as cargo in the hydrophobic core of lipoproteins³.

Cholesterol is often found distributed non-randomly in a specialized type of domain in membranes ; termed "lipid rafts" in a functional state, whereby it exerts many of its actions³. Cholesterol and triglycerides, important lipid constituents of cell, are essential to carry out several vital physiological functions, like maintenance of the structural and functional integrity of all biological membranes and cellular uptake, involved in the activity of membrane bound enzymes and is also important for stabilization of DNA helix. It is an essential constituent of lipoprotein fraction like LDL, HDL and VLDL. Seventy five percent of the plasma cholesterol is transported in the form of LDL. Cells sequester cholesterol from LDL fraction of lipoproteins⁴.

Fates of lipids and lipoproteins - By-products of lipid peroxidation cause marked alteration in the structural integrity and function of cell membranes. Lipid peroxidation by-products formed under physiological and pathological conditions are scavenged by non enzymatic and enzymatic antioxidants. An imbalance between antioxidant defence mechanism and lipid peroxidation processes results in cell and tissue damage⁵.

A positive correlation between vitamin E and lipid peroxidation has been reported in oral cancer pateints. Enhanced lipid peroxidation with decline in antioxidants has been reported in venous blood of oral cancer patients and patients with oral squamous cell carcinoma at different intraoral sites⁵.

Reactive oxygen species play an effective role in the pathogenesis of different pathological diseases, including cancer. Free radical induced lipid peroxidation causes a loss of cell homeostasis by modifying the structure and functions of cell membrane. The most important characteristic of lipid peroxidation is to cause a considerable DNA-MDA adducts by interacting with cellular DNA. However, mammalian cells possess elaborate antioxidant defense mechanisms to neutralize the deleterious effects of free radical induced lipid peroxidation. Enzymatic antioxidants [superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx)] and non-enzymatic antioxidants [vitamin E, reduced glutathione (GSH)] act synergistically with one another to detoxify the effects of lipid peroxidation⁵.

Oral cancer is the sixth most frequent cancer in the world ; some of the highest rates are in developing countries, where up to 25% of all malignancies are found in the oral cavity. In the United States, approx 42000 new cases of head and neck cancer occur annually and result in 12000 deaths. Tobacco is the pre dominant cause of this disease. Alcohol use is a risk factor that acts synergistically with tobacco. Thus, the major risk factor for oral cancer is the same as that for some other common diseases (eg. Emphysema, lung cancer, and heart disease)⁶.

Researchers have reported association of plasma/serum lipids and lipoproteins with different cancers. As neoplastic disease is related to new growth, 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, LDL, or HDL. The plasma concentrations of lipids are not the single additive function of intake, utilization and biosynthesis because of its continuous cycling in and out of the blood stream⁷. The 3rd report of the National cholesterol Education Program (NCEP) expert panel on detection, evaluation and treatment of high blood cholesterol in adults, recommends cholesterol screening in all adults > 20 years. The screening should include fasting lipid profile repeated every 5 years⁸.

NCEP GUIDELINES FOR CLASSIFICATION OF LIPID PROFILE⁸

Lipids constituent	Desirable (mg/dl)	Borderline to High (mg/dl)	High (mg/dl)
Total cholesterol	< 200	200-239	> 240
LDL cholesterol	< 130	130-159	> 160
Triglycerides	< 150	150-499	> 500
HDL cholesterol	> 60	40-59	< 40

Lipid Lipoprotein Normograms in Indian Population and Recommended Level (Mean Value in mg/dL)

	Tg	Choleserol	HDLc	LDLc
Chylomicrons	<0.96	800-500	Alpha-2	>400
East	115	185	42	115
South	155	180	38	107
	119	172	40	108
West	107	188	38	129
North	132	150	43	101
Recommended	≤ 150	≤ 200	≥ 40	≤ 130

Apart from the differences in phospholipids in cancerous and normal tissues, changes in phospholipid metabolism have also been correlated with the severity of various cancers. However, no generalization of the lipid profiles in cancer and normal tissues is possible².

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 malignancies³.

The role of oxidative stress in the genesis of various types of cancer is well established. Antioxidant enzymes and vitamins are important group of cellular constituents responsible for maintaining a balance between oxidants and antioxidants within a cell. Among the intra cellular antioxidant enzymes, superoxide-dismutase (SOD) and Glutathione Peroxidase (GPx) are responsible for the removal of ROS such as superoxide free radicals and H₂O₂. On the other hand, vitamin E breaks free radical chain reactions as a result of their ability to transfer a phenolic hydrogen to a peroxy free radical of a peroxidized polyunsaturated fatty acid (PUFA), thereby preventing peroxidation of PUFA contained in cellular and sub cellular membrane phospholipids. Similarly α -carotene acts as an antioxidant by the stabilization of organic peroxide free radicals within its conjugated alkyl structure. Since α -carotene is effective at low oxygen concentrations, it complements the antioxidant properties of vitamin E which is effective at high oxygen concentration⁹. Therefore, plasma lipid profile levels may be a useful indicator reflecting initial changes occurring in pre-cancerous and neoplastic conditions³.

Hence, the present study is aimed to evaluate the relation between alterations in lipid profiles in different pre-cancerous and neoplastic conditions.

The present study is aimed :-

1. To evaluate plasma lipid profile in untreated patients of squamous cell carcinoma.
2. To evaluate plasma lipid profile in untreated patients of oral submucous fibrosis.
3. To evaluate plasma lipid profile in untreated patients of leukoplakia.
4. To evaluate plasma lipid profile in normal control group.
5. To correlate & evaluate plasma lipid profile in head & neck cancer, oral submucous fibrosis, leukoplakia and normal control group.

METHOD OF DATA COLLECTION AND MEASUREMENTS

160 cases have been taken for current study and comparison of results. Out of which 20 cases have been of oral squamous cell carcinoma, 20 cases have been of oral sub mucous fibrosis, 20 cases have been of leukoplakia and 100 cases have been normal controls.

METHOD OF COLLECTION OF DATA

Detailed case history have been taken and the patients with histopathologically confirmed diagnosis of head &

neck cancer, oral submucous fibrosis and leukoplakia have been included in the study. Fasting blood samples have been taken and collected after centrifugation and then detailed lipid profile have been done. The results have been analyzed using SPSS software. After obtaining informed written consent in prescribed Performa of individual each patient consent form, the collection of primary datasets of serum lipid plasma parameters of OC patient has been collected in Department of Oncology, Geetanjali Cancer Hospital, GMCH, Udaipur. Detailed patient case history has been taken and the patients with confirmed diagnosis of oral cancer patients have been included in this study. Fasting blood samples have been taken and collected after centrifugation. The primary measured serum lipid profile parameters such as Plasma Total Cholesterol (TC, mg/dl), Triglycerides (Trg, mg/dl), High Density Level Cholesterol (HDL, mg/dl) parameters of the collected blood sample of patients were measured by employing the well known and standard Automatic analyzer (M/s BECKMAN COULTER, Model-CX9 PRO). However, on the basis of above measured lipid serum parameters, the LDL Cholesterol (mg/dl) and VLDL Cholesterol (mg/dl) were computed by the well known relations for LDL Cholesterol = TC- Trg- HDL and for VLDL = Trg/5. More details about the principle of the estimation of above discussed serum lipid profile parameters have been already discussed elsewhere (Tietz, N.W., 1995)¹⁰.

Inclusion Criteria

1. The subject were divided into four groups :
 - A. Controls : Healthy persons without any lesions.
 - B. Subjects with leukoplakia : Person with leukoplakia.
 - C. Subjects with OSMF : Person with different grades of OSMF.
 - D. Subjects with squamous cell carcinoma : Person suffering from different grades of squamous cell carcinoma.
2. The subjects were chosen in age groups of 15-55 years of age.
3. The subject's Body Mass Index (BMI) was less than 28.
4. The subjects were on average Indian diet.

Exclusion Criteria

1. Subjects having below mentioned diseases were excluded
 - a) Diabetes Mellitus
 - b) Nephrotic Syndrome
 - c) Alcoholism
 - d) Hypertension
2. Subjects who were on following drugs were excluded
 - a) HMG CO - A reductase Inhibitors
 - b) Fabric acid Derivatives
 - c) Beta blockers
 - d) Nicotinic acid
 - e) Diuretics

3. Subjects who were on diet restriction.

Materials used

1. Gloves, face mask, mouth mirror and probe.
2. Lipid profile reagent kits.
3. Micropipettes for 10µl, 100µl and 1000µl.
4. Centrifuge.
5. Incubator.
6. Autoanalyser.

RESULTS:

When lipid profile of OSMF pts are evaluated against the lipid profiles of healthy control group, the serum levels were lower in OSMF patients than the control group. Statistically, CL values are very highly significant (P = 0.0005), HDL values are very highly significant (P=0.0144), LDL values are very significant (P=0.0017) and TG values are not significant (P=0.245). The results showed that statistically significant difference between squamous cell carcinoma and leukoplakia patients were seen. The mean serum TC (P = 0.24), HDL (P = 0.42), LDL (P = 0.0001) and TG (P = 0.115) values were found to be significantly lowered in squamous cell carcinoma patients than leukoplakia patients (Table - 1 shows comparative results of all the variables serum cholesterol, HDL, LDL and triglycerides in between the control group and other groups

b) When lipid profile of Leukoplakia pts are evaluated against the lipid profiles of healthy control group, the serum levels were lower in leukoplakia patients than control group. Statistically, CL values are very statistically significant (P = 0.0097), HDL values are highly significant (P=0.063), LDL values are statically highly significant (P=0.001) and TG values are not significant (P = 0.201)

c) When lipid profile of squamous cell carcinoma pts are evaluated against the lipid profiles of healthy control group, the serum levels were lowest in squamous cell carcinoma patients than control group. Statistically, CL values are very highly significant (P=0.0046), HDL values are not significant (P=0.606), LDL values are very highly significant (P=0.003) and TG values are significant (P=0.05).

Table - 2 shows comparative results of all the variables serum cholesterol, HDL, LDL and triglycerides in between OSMF and Leukoplakia; values are statistically non-significant.

Table - 3 shows comparative results of all the variables serum cholesterol, HDL, LDL and triglycerides in between OSMF and SCC; values are statistically very high significant for LDL, highly significant for HDL and TG ; significant for CL.

Table -4 shows comparative results of all the variables serum cholesterol, HDL, LDL and triglycerides in between SCC and Leukoplakia ; values are statistically very highly significant for LDL, highly significant for TG and CL ; significant for HDL.

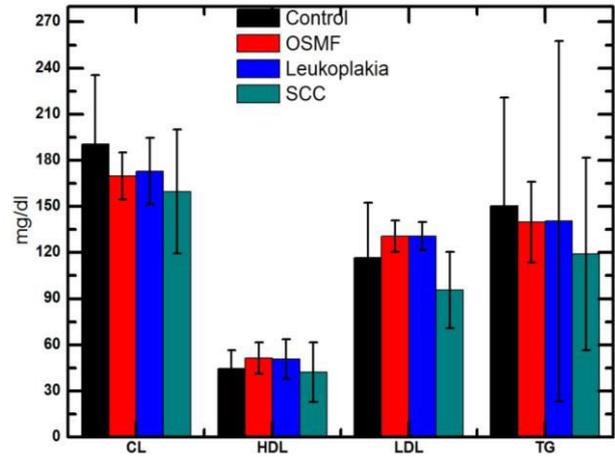


Fig. 1. Histograms show the comparative views of all the serum variables i.e., CL, HDL, LDL and TG in among the control group as well as OSMF, Leukoplakia and SCC group.

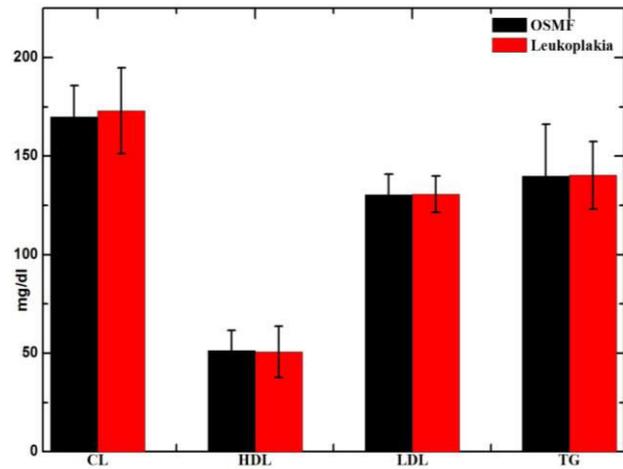


Fig. 2. Histograms illustrate the comparative results of all the variables serum cholesterol, HDL, LDL and triglycerides in between OSMF and Leukoplakia;

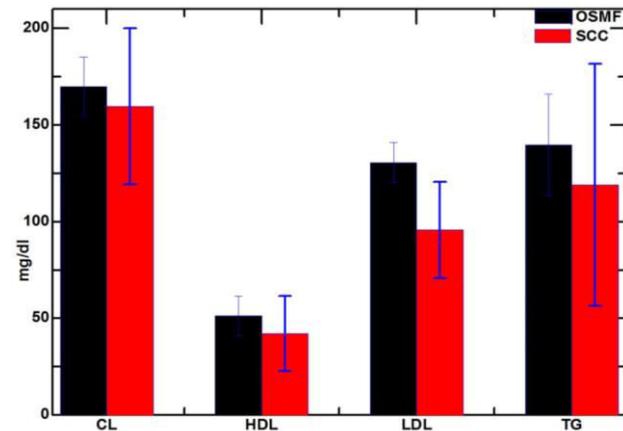


Fig.3 Histogram shows comparative results of all the variables serum cholesterol, HDL, LDL and triglycerides in between OSMF and SCC

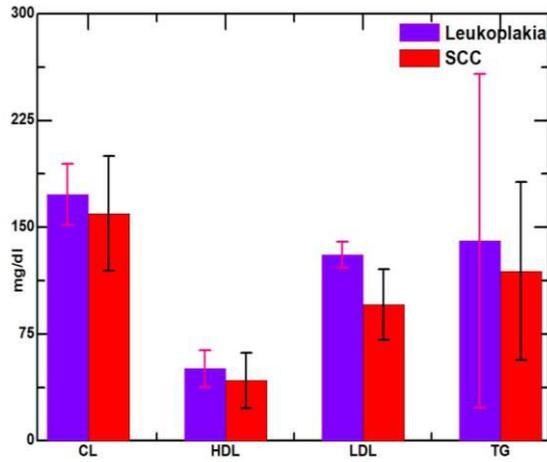


Fig.4 Histogram show shows comparative results of all the variables serum cholesterol, HDL, LDL and triglycerides in between SCC and Leukoplakia

Table -1 Comparison between control group and other groups

Variable	Group	N	M	SD	P Value
CL	Control	100	190.59	44.75	-
	OSMF	20	169.85	15.832	0.0005*
	Leukoplakia	20	172.95	21.693	0.0097*
	SCC	20	159.71	40.28	0.0046*
HDL	Control	100	44.67	12.0	-
	OSMF	20	51.405	10.2864	0.0144*
	Leukoplakia	20	50.770	12.9626	0.063
	SCC	20	42.31	19.45	0.606
LDL	Control	100	116.73	35.63	-
	OSMF	20	130.425	10.2924	0.0017*
	Leukoplakia	20	130.615	9.2162	0.001*
	SCC	20	95.71	24.85	0.003*
TG	Control	100	150.59	70.36	-
	OSMF	20	139.85	26.312	0.245
	Leukoplakia	20	140.30	17.128	0.201
	SCC	20	119.11	62.60	0.05*

Statistical Significant, p<0.05

Table - 2 Comparison of values between OSMF and Leukoplakia

Variable	Group	N	M	SD	P Value
CL	OSMF	20	169.85	15.832	0.971
	Leukoplakia	20	172.95	21.693	
HDL	OSMF	20	51.405	10.2864	0.998
	Leukoplakia	20	50.770	12.9626	
LDL	OSMF	20	130.425	10.2924	1.0
	Leukoplakia	20	130.615	9.2162	
TG	OSMF	20	139.85	26.312	1.0
	Leukoplakia	20	140.30	17.128	

Significant, p<0.05

Table - 3 Comparison of values between OSMF and SCC

Variable	Group	N	M	SD	P Value
CL	OSMF	20	169.85	15.832	0.304
	SCC	20	159.71	40.28	
HDL	OSMF	20	51.405	10.2864	0.07
	SCC	20	42.31	19.45	
LDL	OSMF	20	130.425	10.2924	0.0001*
	SCC	20	95.71	24.85	
TG	OSMF	20	139.85	26.312	0.18*
	SCC	20	119.11	62.60	

Significant, p<0.05

Table – 4: Comparison of values between Leukoplakia and SCC

Variable	Group	N	M	SD	P Value
CL	Leukoplakia	20	172.95	21.693	0.24
	SCC	20	159.71	40.28	
HDL	Leukoplakia	20	50.770	12.9626	0.42
	SCC	20	42.31	19.45	
LDL	Leukoplakia	20	130.615	9.2162	0.0001*
	SCC	20	95.71	24.85	
TG	Leukoplakia	20	140.30	17.128	0.115
	SCC	20	119.11	62.60	

Significant, p<0.05

DISCUSSION

Several retrospective and prospective studies have shown an inverse relation between serum cholesterol levels and squamous cell carcinoma and PMD incidence. No causative relation has been established nevertheless, so far, and some believe that hypocholesterolemia is, in fact, the result rather than the cause of cancer and PMD. According to Alexopoulos et al (1987)¹¹, irrespective of which hypothesis is correct, one would expect hypocholesterolemia and associating lipoprotein disorders to be constant findings in untreated cancer patients.

In our study, first lipid profile of OSMF patients was evaluated against the lipid profile of healthy individuals. The results showed statistically significant difference between controls and OSMF patients. The mean serum TC (P=0.0005), HDL (P= 0.0144), LDL (P=0.0017) and TG (P=0.245) values were found to be significantly lowered in OSMF patients than controls (Table-1 and Fig.-1). These results were complementary to the studies done by Kritchevsky SB et al (1991)¹² who found no clear relationship between cancer diagnosis and patterns of change for triglycerides and high density lipoprotein cholesterol; Patel PS et al (2004)⁴ reported significant decrease in plasma total cholesterol and HDLC in patients with Oral pre-cancerous condition (P=0.014 and P = 0.000, respectively) as compared to the controls. The VLDLC and triglycerides levels were lower in patients with Oral pre-cancerous condition as compared to the controls (P=0.04). They concluded that there was significantly low level of HDLC in patients with Oral pre-cancerous condition as compared to controls. According to these results, they concluded that there was a significant decrease in VLDLC & Triglyceride level in patients with Oral pre-cancerous condition compared to controls; Mehrotra R et al. (2009)³ conducted a study on 60 OSMF patients and found a significant increase in serum total cholesterol, LDL, VLDL and triglycerides levels, significant decrease in HDL. According to these results they came on a conclusion that the lower levels of plasma cholesterol and other lipid constituents in patients might be due to their increased utilization ; Lohe V K et al (2009)¹³ reported a significant decrease in TC, VLDL and HDL in Oral pre-cancer group as compared to control. They reported an inverse relationship between serum lipid profile and Oral pre-cancer; Nayak p et al (2010)¹⁴ reported that 3 parameters (TC, HDL and LDL) of lipid profile were

reduced in Oral Pre-cancerous cases as compared to age and sex matched healthy controls. They said estimation of lipid profile can be considered as a good marker for increased cell turnover.

Then lipid profile of leukoplakia patients were evaluated against the lipid profile of healthy individuals. The results showed statistically significant difference between controls and leukoplakia patients. The mean serum TC (P = 0.0097), HDL (P = 0.063), LDL (P = 0.001) and TG (P = 0.201) values were found to be significantly lowered in leukoplakia patients than controls (Table-1 and Fig.-1). These results were complementary to the studies done by Kritchevsky SB et al (1991)¹² who found no clear relationship between cancer diagnosis and patterns of change for triglycerides and high density lipoprotein cholesterol ; Patel PS et al (2004)⁴ reported significant decrease in plasma total cholesterol and HDLC in patients with Oral pre-cancerous condition (P = 0.014 and P = 0.000, respectively) as compared, to the controls. The VLDLC and triglycerides levels were lower in patients with Oral pre-cancerous condition as compared to the controls (P=0.04). They concluded that there was significantly low level of HDLC in patients with Oral pre-cancerous condition as compared to controls. According to these results, they concluded that there was a significant decrease in VLDLC & Triglyceride level in patients with Oral pre-cancerous condition compared to controls ; Lohe V K et al (2009)¹³ reported a significant decrease in TC, VLDL and HDL in Oral pre-cancer group as compared to Control. They reported an inverse relationship between serum lipid profile and Oral pre-cancer; Nayak P et al (2010)¹⁴ reported that 3 parameters (TC, HDL and LDL) of lipid profile were reduced in Oral Pre-cancerous cases as compared to age and sex matched healthy controls. They said estimation of lipid profile can be considered as a good marker for increased cell turnover.

Then lipid profile of OSMF patients were evaluated against the lipid profile of leukoplakia patients. The results showed no statistically significant difference between OSMF and leukoplakia patients. The mean serum TC (P = 0.97), HDL (P = 0.99), LDL (P = 1.0) and TG (P = 1.0) values were found to be similar in OSMF and leukoplakia patients (Table-2 and Fig. -2). These results were complementary to the studies done by most of the authors, which concluded that there is no

significant difference between the changes in lipid profile of OSMF and leukoplakia patients.

Then lipid profile of squamous cell carcinoma patients were evaluated against the lipid profile of healthy individuals. The results showed statistically significant difference between controls and cancer patients. The mean serum TC (P=0.0046), HDL (P=0.606), LDL (P=0.003) and TG (P=0.05) values were found to be significantly lowered in cancer patients than controls (Table-1 and Fig.-1). These results were complementary to the studies done by Gerhardsson M. et al (1986)¹⁵ reported that the low serum cholesterol levels were an effect of the cancer in an early stage and not vice versa; Alexopoulos C G et al (1987)¹¹ studied serum cholesterol and its fractions, serum triglycerides, and serum lipoproteins in patients with various malignancies in comparison with age-matched controls. They reported that cancer patients as a group demonstrated significantly lower total cholesterol, esterified cholesterol and LDL, compared with controls; Schatzkin A et al (1988)¹⁶ studied the relation of total serum cholesterol to all cancer and site-specific cancer incidence and found an inverse association between Cholesterol and all cancer, lung, colorectal, pancreatic and bladder cancers; and leukemia; Albeatici S et al (1989)¹⁷ reported that low blood cholesterol is a factor favouring the onset of cancer; Cowan L D (1989)¹⁸ reported that total cholesterol and low-density lipoprotein (LDL) cholesterol were significantly inversely associated with overall cancer mortality in men, but no relation was observed in women. Neither high-density lipoprotein (HDL) cholesterol nor triglycerides were significantly related to total cancer mortality in either sex, although in women, HDL cholesterol was positively associated with risk of death from gynecologic cancers; Kritchevsky SB et al (1991)¹² reported no clear relationship between cancer diagnosis and patterns of change for triglycerides and high density lipoprotein cholesterol; Camps E S et al (1998)¹⁹ reported that serum cholesterol observed in the patients with cancer were lower than the ones observed in the healthy controls; Rywik S L et al (1999)²⁰ reported that relative risk of cancer mortality was highest and significant at the lowest HDL cholesterol level in the US and Poland. But Cancer mortality was not significantly related to triglycerides. They concluded that relations of total and cancer mortality with lipids or lipoproteins are weaker than associations with cardiovascular mortality; Raste A S et al (2000)²¹ reported that total lipids, cholesterol and HDL cholesterol levels are inversely associated with incidence of cancer where as triglycerides levels were significantly elevated in cancer patients; Patel PS et al (2004)⁴ reported a significant decrease in plasma total cholesterol and HDLC in cancer patients (P = 0.008 and P = 0.000, respectively) as compared to the controls. The VLDLC and triglycerides levels were lower in cancer patients as compared to the controls (P = 0.059). Plasma LDLC levels did not reveal any significant difference. They concluded that there was significantly low level of HDLC, VLDLC & Triglyceride in cancer patients

compared to controls; Tomiki Y et al (2004)²² reported TC and LDL-C were significantly lower in cancer-bearers by approximately 15 mg/dl. Furthermore, analysis by cancer site also showed significantly lower TC and LDL-C levels in cancer-bearers than in controls for all three sites. Early stage cancer-bearers showed a significant decrease in TC levels by approximately 11 mg/dl. compared with controls, and also a similar decrease in LDL-C levels. According to results they suggested that low TC levels are not related to cancer stage; Preetha A et al (2005)² reported that the phosphatidylglycerol level in cancerous cervical tissue was nearly five folds higher than that in normal cervical tissue; Qadir M I et al (2006)²³ observed plasma lipid profile (triglycerides, cholesterol, LDL-cholesterol and HDL-cholesterol) in sarcoma patients. Their results showed that sarcoma patients showed highly significant (P<0.01) decrease, when compared with the normal control subjects; Lohe V K et al (2009)¹³ reported significant decrease in TC, HDL, VLDL, and triglyceride in Oral Cancer group as compared to Control. Also an inverse relationship between serum lipid profile and Oral Cancer; Nayak P et al (2010)¹⁴ reported that 3 parameters (TC, HDL and LDL) of lipid profile were reduced in Oral cancer cases as compared to age and sex matched healthy controls. And the estimation of lipid profile can be considered as a good marker for increased cell turnover.

LEUKEMIAS - Budd D and Ginsberg H (1986)²⁴ determined plasma total, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol concentrations in 32 patients admitted with either acute nonlymphocytic leukemia or chronic myelogenous leukemia. They reported that plasma total, LDL, and HDL cholesterol levels in 15 male (111.9 f 27.9; 53.7 f 10.4; 23.7 f 22.5 mg/dl) and 17 female (124.0 f 42.0; 68.6 f 32.0; 29.4 f 13.9 mg/dl) patients were markedly reduced compared with age and sex-matched control values (all P < 0.01). They concluded that LDL cholesterol concentrations may be of value in assessing disease activity in individuals with acute myelogenous leukemia; Halton J M et al (1998)²⁵ observed an altered blood lipid profile in patients of acute lymphoblastic leukemia (ALL). Statistically significant values included elevated triglycerides (1.82 f 1.23 mmol/L), reduced HDL-C (0.54 f 0.24 mmol/L), and reduced apolipoprotein -A (ApoA) (0.77 f 0.18 g/L) levels.

BREAST CANCERS - Boyd NF et al (1990)²⁶ reported evidence of association between plasma high-density lipoprotein cholesterol and risk factors for breast cancer. They suggested an association between high HDL-C levels and the epidemiology of breast cancer risk; Collins T A et al (1998)²⁷ concluded that significant correlation between the high levels of triglycerides and breast cancer risk (odds ratio 5.12) may be attributed to differences in lipid metabolism between the women with breast cancer and controls, or to the consequences of breast cancer; Chang S J et al (2007)²⁸ demonstrate that higher VLDL-C and lower apo A-I values were significantly associated with breast cancer; Fiorenza A M et al (2007)²⁹ reported

that total cholesterol, low-density lipoprotein-cholesterol, high-density lipoprotein-cholesterol, serum albumin, and body mass index were significantly lower in cancer than in non cancer-subjects. The lowest values of total cholesterol, low-density lipoprotein cholesterol and high-density lipoprotein-cholesterol were recorded in patients with haematological malignancies and the highest in patients with breast tumor. Vyas T et al³² (2016) reported that The observed lower p values lower than 0.04 also give furthermore confirmation and statistical support about the validity of clear reduction in lipid profile squamous cell carcinoma patients than in non-oral cancer group . The lower plasma lipid status may be a useful bio-marker indicator for initial changes occurring in neoplastic cells. Plasma TC, HDL, LDL and Trg values were found to be lower in oral squamous cell carcinoma relative to non-oral patient category.

Then lipid profile of OSMF patients were evaluated against the lipid of squamous cell carcinoma patients. The results showed statistically significant difference between squamous cell carcinoma and OSMF patients. The mean serum TC (P = 0.304), HDL (P = 0.07), LDL (P = 0.0001) and TG (P = 0.18) values were found to be significantly lowered in squamous cell carcinoma patients than OSMF patients (Table-3 and Fig.-3). These results were complementary to the studies done by Kritchevsky SB et al (1991)¹² analysed changes in lipoprotein cholesterol, total plasma cholesterol, and weight prior to the diagnosis of cancer. They found no clear relationship between cancer diagnosis and patterns of change for triglycerides and high density lipoprotein cholesterol ; Patel PS et al (2004)⁴ reported significant decrease in plasma total cholesterol and HDLC were observed in cancer patients (P = 0.008 and P = 0.000, respectively) as well as in patients with Oral pre-cancerous condition (P = 0.014 and P = 0.000, respectively) as compared to the controls. The VLDLC and triglycerides levels were lower in cancer patients as compared to the controls (P = 0.059) as well as the patients with Oral pre-cancerous condition (0.04).

According to these results, they concluded that there was a significant decrease in HDLC, VLDLC & Triglyceride level in cancer patients compared to controls and patients with Oral pre-cancerous condition; Lohe V K et al (2009)¹³ reported a significant decrease in TC, VLDL and HDL in Oral cancer group and Oral pre-cancer group as compared to Control, But the decrease was more in Oral cancer group than the Oral pre-cancer group. They reported an inverse relationship between serum lipid profile and Oral Cancer and Oral pre-cancer groups.

Then lipid profile of leukoplakia patients were evaluated against the lipid profile of squamous cell carcinoma patients. The results showed that statistically significant difference between squamous cell carcinoma and leukoplakia patients were seen. The mean serum TC (P = 0.24), HDL (P = 0.42), LDL (P = 0.0001) and TG (P = 0.115) values were found to be significantly lowered in squamous cell carcinoma patients than leukoplakia

patients (Table-4 and Fig.-4). These results were complementary to the studies done by Kritchevsky SB et al (1991)¹² analysed changes in lipoprotein cholesterol, total plasma cholesterol, and weight prior to the diagnosis of cancer. They found no clear relationship between cancer diagnosis and patterns of change for triglycerides and high density lipoprotein cholesterol ; Patel PS et al (2004)⁴ reported significant decrease in plasma total cholesterol and HDLC were observed in cancer patients (P = 0.014 and P = 0.000, respectively) as compared to the controls. The VLDLC and triglycerides levels were lower in cancer patients as compared to the controls (P = 0.059) as well as the patients with Oral pre-cancerous condition (0.04). According to these results, they concluded that there was a significant decrease in HDLC, VLDLC & Triglyceride level in cancer patients compared to controls and patients with Oral pre-cancerous condition; Lohe V K et al (2009)¹³ reported a significant decrease in TC, VLDL and HDL in Oral cancer group and Oral pre-cancer group as compared to Control. But the decrease was more in Oral cancer group than the Oral pre-cancer group. They reported an inverse relationship between serum lipid profile and Oral Cancer and Oral pre-cancer groups.

The results are strengthened by the present study showing lower plasma TC, HDL, LDL and TG in squamous cell carcinoma, OSMF and leukoplakia patients than healthy individuals. The theoretical explanation for this is that, in malignant conditions, blood cholesterol undergoes early and significant changes. Low levels of cholesterol in the proliferating tissues and in blood compartments could be due to process of carcinogenesis and dysplastic changes. This Hypolipidemia may result due to the direct lipid lowering effect of tumour cells, use of lipids in fast and excessive cell multiplication or some secondary malfunction of the lipid metabolism or secondary to antioxidant vitamins.

Tobacco carcinogens induce generation of free radicals and reactive oxygen species³⁰; while excessive use of areca nut may cause fibrosis due to increased synthesis of collagen and induce the production of free radicals and reactive oxygen species³¹; which are responsible for high rate of oxidation/peroxidation of polyunsaturated fatty acids. This peroxidation further release peroxide radicals. This affects essential constituents of the cell membrane and might be involved in carcinogenesis/tumorigenesis^{30,31}. Because of the lipid peroxidation, 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, LDL or HDL^{30,31}. Researchers have reported association of plasma/serum lipids and lipoproteins with different cancers. As neoplastic disease is related to new growth, there is a greater utilization of lipids including total cholesterol, lipoproteins and triglycerides for new membrane biogenesis. Apart from the differences in phospholipids in cancerous and normal

tissues, changes in phospholipid metabolism have also been correlated with the severity of various cancers. Plasma lipid profile levels may be a useful indicator reflecting initial changes occurring in pre-cancerous and neoplastic conditions. The lower plasma lipid status may be useful bio-marker indicator for initial change occurring in neoplastic cells.

CONCLUSIONS:

1. The lower plasma lipid status may be a useful indicator for initial changes occurring in neoplastic cells. Plasma TC, HDL, LDL and TG values were lower in squamous cell carcinoma, OSMF and leukoplakia patients than healthy individuals. The most reduced levels are present in cancer patients while OSMF and Leukoplakia patients have similar levels.
2. There was statistically significant difference present in lipid profile of OSMF, leukoplakia and squamous cell carcinoma patients than in normal groups.
3. There was no statistically significant difference present between lipid profile of OSMF and leukoplakia patients.
4. Lipid profile of squamous cell carcinoma was lower than OSMF patients.
5. Lipid profile of squamous cell carcinoma was lower than leukoplakia patients.

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