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Serum lipid profile alterations in oral potentially malignant disorders and oral squamous cell carcinoma- cross sectional study in a govt dental hospital in eastern India

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Abstract

Context: Lipids are major cell membrane components essential for various biological functions, including cell growth and division of normal and malignant tissues.

Aims: To study the role of serum lipid profile alteration in patients with Oral potentially malignant disorders (OPMD) & Oral squamous cell carcinoma (OSCC) and to also correlate it with tobacco habit for understanding its predictive role in prognosis of this disease.

Setting & Design: Comparative case control study was carried out in 60 clinically & histopathologic ally diagnosed cases of OPMD & OSCC each and 30 healthy individuals treated as controls.

Methods and Material: Serum lipids including: (i) Total cholesterol (TC), (ii) Low density Lipid (LDL) cholesterol, (iii) High Density Lipid (HDL) cholesterol (iv) Very Low-Density Lipid (VLDL) cholesterol and (v) triglycerides (TG) were analyzed in patient samples and that of controls by spectrophotometry.

Statistical analysis used: Inter group comparison (>2 groups) was done using one way ANOVA followed by pair wise comparison using post hoc test (SPSS v 21.0,

IBM).

Results: Statistically significant & negative correlation were seen between the groups pertaining to TC, HDL, LDL, which indicates that as we progress in the groups from control through OPMD to OSCC there is a decrease in the values of serum lipid profile. Serum TC, TG, HDL, LDL and VLDL levels were found to decrease with increasing grades of OSCC, with lowest values seen in poorly differentiated OSCC.

Conclusion: There is evidence of an inverse relationship between the serum lipid profile values of OSCC and OPMD.

Keywords: OSCC, OPMD, Serum Lipid profile, Biochemical marker, Serum cholesterol, LDL, HDL, VLDL.

Key Messages: The findings of this study suggest that serum lipid profile may be used as a biochemical marker for progression of OPMD and OSCC and as a indicator for initial changes occurring in neoplastic cells.

Introduction

Oral cancer (OC) is the eighth most common head and neck cancer in the world having an overall 5-year survival rate of less than 50%.[1-3] This accounts for an estimated 650,000 new cancer cases and 350,000 cancer deaths globally every year.[4-6] The majority of OSCC cases are preceded by precursor lesions, collectively referred to as OPMDs.[7,8] A variety of lesions and conditions have malignant potentiality which may include leukoplakia, erythroplakia, oral lichen planus and oral submucous fibrosis.[9] The mutagenic effects of prevalent habits of tobacco, alcohol, betel quid or areca-nut are dependent upon dose frequency and duration of use.[10-12]

Biochemical studies in evaluation of cancer have shown that various substances alter quantitatively in the serum during tumour development collectively referred to as tumour markers, one such marker being the Serum Lipid profile.[1,13,14] It is believed that tobacco carcinogens induce generation of free radicals and reactive oxygen species which is responsible for high rate of oxidation or peroxidation of poly-unsaturated fatty acids.[15,16]

Previous research reports strong correlation between serum lipids and lipoproteins and several carcinomas including colon, breast, ovarian and prostrate, providing a founding base for epidemiological research in OSCC.[17]

The present study was therefore undertaken to evaluate the implications of altered Serum Lipid Profile in patients with OPMD and OSCC visiting our Government Dental Hospital.

Materials and methods

Sample size and selection criteria: The patient samples for the present comparative cross-sectional study were randomly selected from the patients attending the Out Patient Department (OPD) of Dept. of Oral Medicine & Radiology at our Government Dental College & Hospital under required norms, regulations & ethical committee clearance.

The sample size of this study comprised of 60 clinically & histopathologic ally diagnosed cases of OPMD (as per WHO 2015 criteria) and OSCC each - that reported from a period between 2016 to 2018 (Group II & III respectively). 30 age and sex matched healthy individuals were included as controls (Group I). A written consent was obtained from patients and controls after explaining the significance of this study and the procedures involved. There were 14 patients of Oral Leukoplakia, 11 patients of Oral Lichen planus and 5 patients of OSMF comprising Group II. Patients in the age group of 25-75 years, irrespective of sex and with a willingness to participate were included in the study. A detailed case history was recorded and thorough clinical examination was carried out for all subjects. Routine

hematological investigations including were performed for all patients to rule out other systematic diseases. OPMD and OSCC were confirmed after histopathological diagnosis.

The OSCC group was histologically classified as per Broder's grading into well, moderately, and poorly differentiated carcinomas.[18,19]

The subjects in each group were further classified according to presence or absence of tobacco habit: NHT- No habit of any form of tobacco consumption, WHT- With habit of tobacco consumption in one or the other form (smoking, chewing, snuff); as per Lohe et al[14]study.

Patients having systemic diseases which affected the serum lipid levels like Obesity, Nephrotic syndrome, Thyroid disorders, Diabetes Mellitus and Renal disorder were excluded.

Blood sample collection

The vein near antecubital fossa was exposed and punctured using a 2 ml sterile disposable plastic syringe and 24-gauge needle; 2 ml of overnight fasting blood sample was drawn & collected in plain vials. These samples were allowed to clot and the supernatant transferred to a disposable vial for assay. The estimation was performed using kits obtained from ERBA diagnostics (Trans Asia Bio-Medicals Ltd., Mumbai, India).

Lipid analysis

Based on the spectrophotometric principle, lipid analysis was carried out with a semiautomated machine (Erba Chem-5 plus v2), using an ultra violet (UV) – visible spectro photo meter. Quantitative estimation of serum lipid profile was performed by a reagent kit (Accurex biomedical pvt. Ltd). Serum lipid profile in the form of total cholesterol (TC), high-density lipoprotein-cholesterol (HDLC) and triglycerides (TGL) were analyzed as per manufacturer's guidelines, on the same day of the collection of the sample.

For serum cholesterol and serum TGL, following addition of 1000µL of cholesterol/ TGL reagent to 3 test tubes of 10 µL of serum sample, distilled water and cholesterol/ TGL standard each, the mixtures were incubated at 37 °C for 10 minutes and the absorbance of standard and sample was measured against a blank at 505 nm in the analyzer.

For serum HDLC measurement, 250 µL of serum sample was mixed with 500 µL of HDL precipitating reagent, followed by 10 min incubation at room temperature followed by centrifugation at 4000 rotation per minute (rpm) for 10 mins to obtain a clear supernatant. 50 µL of this supernatant was subjected to addition of 1000 µL of cholesterol reagent followed by incubation and measurement as before for the other lipids.

The LDLC and VLDLC levels were calculated from formulas as shown below:

- LDLC = Total cholesterol – (VLDLC) – (HDLC)
- VLDLC = Triglycerides/5

Comparison of lipid profiles in different types of OPMD and various grades of OSCC and their correlation with tobacco habit was made.

Statistical analysis

All analysis was performed using the Statistical package for social sciences (SPSS v 21.0, IBM). Descriptive statistics like frequencies and percentage for categorical data, Mean & SD for numerical data has been depicted. Inter group comparison (2 groups) was done using t test. Inter group comparison (>2 groups) was done using one way ANOVA followed by pair wise comparison using post hoc test. Comparison of frequencies of categories of variables with groups was done using chi square test. For all the statistical tests, $p<0.05$ was considered to be statistically significant, keeping α error at 5% and β error

at 20%, thus giving a power to the study as 80%.

Results

The present study revealed a strong association between the serum lipid profiles of patients with OPMD & OSCC.

The mean age of subjects was compared between the groups and it was found that there was a statistically non-significant difference seen for the mean age between the groups (p>0.05). Also, on comparison of frequencies of gender between the groups, there was a statistically non-significant difference seen for the frequencies between the groups (p>0.05) indicating that the distribution of subjects as per age and gender was equal among the 3 groups.

However, there was a statistically highly significant difference seen for the frequencies of subjects when compared with various groups as per tobacco habits (p<0.01) with higher number of subjects i.e. (n=22/30) in controls with NHT and higher number of WHT in OPMD (n=24/30) and OSCC (n=27/30) [Table 1]

Table 1: Demographic details

		Frequency	Percentage
Age	Mean 45.60 ± 11.952 years		
Gender	M	52	57.8
	F	38	42.2
Tobacco habits	NHT	31	34.4
	WHT	59	65.6
Site occurrence	Alveolo-buccal complex	12	40.0
	Alveolus	8	26.7
	Buccal mucosa	5	16.7
	Retromolar area	2	6.7
	Tongue	3	10.0
Grades	Well differentiated SCC	14	46.7
	Moderately differentiated SCC	13	43.3
	Poorly differentiated SCC	3	10.0

NHT- No Habit of Tobacco, WHT- With habit of tobacco

A marked decrease in serum TC (122.42± 21.47), TG (122.45±23.42), HDL (31.81±5.26), LDL (66.10±18.71) and VLDL (24.49±4.64), was seen in the OSCC group when compared with the OPMD group in our study. There was a statistically significant difference seen for the values between the groups (p<0.01, 0.05) with higher TC, HDL, LDL in controls, while higher TG & VLDL in OPMD group. [Table 2] On pairwise comparison using Tukeys post hoc tests, it was found that there was a statistically significant seen for the values between the pairs of groups (p<0.01, 0.05) for the variables i.e. TC, HDL & LDL between all pairs of groups, while for TG & VLDL between OPMD & OSCC.

Table 2: Inter group comparison OF SERUM LIPID PROFILE (n=30 per group)

		Mean	Std. Deviation	Std. Error	F value	p value
TC	Controls	173.30	24.74	4.51		
	OPMD	145.26	23.87	4.35	35.56	0.000**
	OSCC	122.42	21.47	3.92		
TG	Controls	129.84	22.98	4.19		
	OPMD	138.84	26.41	4.82	3.41	0.037*
	OSCC	122.45	23.41	4.27		
HDL	Controls	40.53	6.00	1.09		
	OPMD	36.61	4.62	.84	20.15	0.000**
	OSCC	31.81	5.26	.96		
LDL	Controls	107.01	18.96	3.46		
	OPMD	80.87	20.29	3.70	34.43	0.000**
	OSCC	66.10	18.71	3.41		
VLDL	Controls	25.97	4.62	.84		
	OPMD	27.77	5.25	.95	3.43	0.037*
	OSCC	24.49	4.64	.84		

Values expressed as mean in mg/dl

There was a statistically significant & negative correlation seen between the groups vs TC, HDL, LDL which indicates that as we move in the group number i.e. from 1 to 3 there is a decrease in the blood variables. [Table 3]

Table 3: Correlation between various forms of serum lipid profile and groups - Controls, OPMD & OSCC

		TC	TG	HDL	LDL	VLDL
Groups	Correlation co-efficient (r value)	-.669**	-.122	-.562**	-.656**	-.122
	p value	0.000	0.254	0.000	0.000	0.253
	N	90	90	90	90	90

There was a statistically non-significant difference seen for the values between the groups (p>0.05) also on pairwise comparison using Tukeys post hoc tests. There was a statistically non-significant difference seen for the values between all pairs of groups (p>0.05) [Table 4]

Table 4: Comparison with grades in OSCC group

	Grades	N	Mean	Std. Deviation	Std. Error	F value	p value
TC	1	14	122.87	20.53	5.48		

	2	13	127.62	21.75	6.03	2.61	0.09#
	3	3	97.80	4.65	2.68		
TG	1	14	118.02	26.50	7.08		
	2	13	129.76	20.37	5.65	1.23	0.30#
	3	3	111.40	15.02	8.67		
HDL	1	14	31.70	5.96	1.59		
	2	13	32.48	4.83	1.34	.40	0.67#
	3	3	29.40	4.24	2.45		
LDL	1	14	67.50	16.82	4.49		
	2	13	69.21	20.37	5.64	2.07	0.14#
	3	3	46.13	8.44	4.87		
VLDL	1	14	23.65	5.27	1.40		
	2	13	25.92	4.01	1.11	1.20	0.31#
	3	3	22.26	3.02	1.74		

There was a statistically significant difference seen for the serum lipid profile between the groups with tobacco habits ($p<0.01, 0.05$) with higher TC, TG, HDL, LDL & VLDL in NHT group as compared to WHT group. [Table 5]

Table 5: Comparison of serum lipid profile with tobacco habits

	Tob Hab	N	Mean	Std. Deviation	Std. Error Mean	T value	p value of t test
TC	NHT	31	172.34	25.87	4.64	6.89	0.000**
	WHT	59	133.68	24.97	3.25		
TG	NHT	31	138.24	22.73	4.08	2.21	0.029*
	WHT	59	126.24	25.28	3.29		
HDL	NHT	31	38.96	6.86	1.23	2.98	0.004**
	WHT	59	34.92	5.67	.73		
LDL	NHT	31	105.93	19.64	3.52	7.14	0.000**
	WHT	59	73.49	20.89	2.71		
VLDL	NHT	31	27.65	4.53	.81	2.21	0.029*
	WHT	59	25.25	5.04	.65		

Discussion

OSCC comprises about 90–95% of all oral malignancies, and hence the term ‘oral cancer’ is used in a restricted

sense to describe OSCC.[20] The mechanism of carcinoma development is complex and involves an inter-play between intricate processes comprising of proliferation, apoptosis, and differentiation that determines tumour development and progression.[21] Rapidly proliferating cancer cells require increased amounts of lipids for enhanced signaling and resistance against apoptosis.[22]

Lipids are a diverse class of biomolecules known to play a key role in cellular energy storage, structure, and signalling.[22] Most dietary lipids are in the form of triglycerides (TG), total cholesterol (TC) and phospholipids.[3,23]Cholesterol is essential for maintenance of the structural and functional integrity of all biological membranes. TG and cholesterol are packaged into lipoproteins and transported in the plasma, which are then taken up and degraded by cells to fulfill the demands for cellular functions.[15,24]

Data retrieved from studies that relate dyslipidemias with cancer development remain elusive. It has been proposed that hypolipidemia may be a predisposing factor for cancer development although no causative relationship has been established so far. However, some researchers have suggested that an aberrant lipid profile and hypolipidemia in cancer patients is a consequence rather than cause of cancer.[21]

Various studies have found significantly lower levels of TC, HDL & LDL in oral cancer compared to controls[21] whilst some have found a significant decrease in TC, HDL, VLDL and TG but not in LDL in OSCC patients compared with the control group.[14,15,25] Others have found non-significant differences in VLDL levels between the two groups.[21,26,27] Findings of current study are in agreement with most as there was a significant decrease across all serum lipid values in OSCC as compared to controls.

Studies have reported a marginal or no decrease in serum TC and HDL with loss of tumour differentiation.[14,21] Sherubin et al observed a progressive decline in TC levels, with the lowest levels seen in poorly differentiated lesions and concluded that this was a result of the differential utilization of lipids by different grades of lesion.[28] This finding was reiterated in lowered serum lipid values of current study. Krontiras & Roye[29] stated that differential utilization of plasma lipids by the malignant cells can be explained by the fact that the enzyme fatty acid synthase which is necessary for the synthesis of fatty acid increases as the differentiation of the cell decreases. The enzyme fatty acid synthase and its activity are highly elevated in biosynthetically altered anaplastic cells of poorly differentiated lesions as compared to moderate and well differentiated carcinoma.[28] Rationally, the levels of lipid profile fractions should decrease constantly as the grade of OSCC increases.[3]

Explanations cited in the literature to support hypocholesterolemia as a consequence of cancer range from an ongoing process of oncogenesis leading to direct lipid lowering effect of tumour cells or some secondary malfunction of the lipid metabolism or secondary to antioxidant vitamins, increased lipid utilization due to new membrane formation, cell growth and division.[3] Yet another postulated mechanism for lower levels of serum cholesterol in cancer patients states that there is increased membrane permeability to carcinogens induced by trans-fatty acids.[14]

Since oral squamous cell carcinoma is more often preceded by oral precancerous conditions (Oral leukoplakia, Oral lichen planus, OSMF), an attempt was made to analyse the various forms of serum lipid levels in OPMDs as well.

Kumar et al found marked decrease in serum HDL ($p< 0.027$) & LDL ($p< 0.005$) levels between OSCC and leukoplakia but no significant differences between LKP and controls though levels of TC, HDL and LDL were lower in the former. Few authors have found correlation between mean lipid values and the degree of dysplasia.[14,21] They inferred that perhaps hypolipidemias is a late event in carcinogenesis. Some authors found significantly lower levels of TC and HDL in various oral precancers/ OPMD compared with controls[14,15,25,30] which was similar to our findings that additionally also observed lowered levels of LDL. However, mean TG and VLDL were higher than controls as also observed in studies of Mehrotra et al[31] that found higher serum VLDL levels in oral precancer compared to controls and Mehdipour[32] who found higher lipid profile in 44 OLP patients as against 44 controls. Few studies found marked decrease in all the serum lipid values(TC, TG, HDL, LDL and VLDL) in OSMF compared to controls with most significant reduction in higher stages of OSMF.[17,33] Other authors have found significantly lowered levels of TC and HDL in OSMF.[12,31,34] In contrast, Sharma et al[13] observed increased levels of serum HDL in OSMF. Mehdi pour et al[32], Jornet et al[35]found mean serum levels of triglycerides were higher in erosive and non-erosive OLP patients compared to healthy subjects while the latter in a sample of 400 cases, found significantly lowered levels of HDL in OLP compared to controls ($p<0.005$). The presence of inflammatory processes may explain the possible link between OLP and dyslipidemia.[35] However, in contrast to this, Gupta et al[30] found serum TC significantly higher in oral leukoplakia and oral lichen planus group as compared to OSCC. Such increase in serum cholesterol and triglycerides may be explained due to increased abundance in the size of lipid raft domains in oral lichen planus. Our observations of significantly lower values of TC, HDL and LDL in OSCC as compared to OPMD is in accordance with findings of most studies.[14,15,26] This is in conflict with a study reporting higher HDL and TG levels in OSCC than OPMD.[30]

The results of the present study are in accordance with various studies conducted elsewhere[14,20,26,36] These results indicate that changes in serum lipid profile levels are not specific to any type of cancer, but relate to cancer in general. This further also explains why the lipid components also decrease in different cancer types.[36]

There is a strong relationship between vitamin E (a liposoluble antioxidant vitamin) and lipids, especially cholesterol. Vitamin E is co transported with all forms of cholesterol and contributes to the first line of defense against lipid peroxidation. Further, triglycerides and cholesterol are positively correlated with vitamins.[37,38]

Mean TC & HDL values were significantly lesser in all forms of tobacco users without lesions compared to controls.[15,21] An explanation for the same is that tobacco induces free radical and ROS generation leading to high rate of peroxidation of PUFA and increased lipid utilization. Lipid peroxidation products may cross link DNA contributing further to carcinogenicity and mutagenicity. Lohe et al[14] in study of a large sample of 210 cases with habit wise distribution, however found no significant correlation of serum lipid profile and tobacco use. Current study showed significantly lesser values of assessed serum lipids in tobacco habituates than non-habit group. However, these results are confounded by the fact that the WHT cohort were primarily seen in those harboring OPMD or OSCC (51/59) and the controls mainly constituted those without habits (22/31 NHT). It is difficult to elucidate if the serum lipid values are a reflection of effects of tobacco or the process of carcinogenesis.

Moreover, Rose and Shipley[24] have reported 66% higher mortality rate because of cancer in cancer patients with lowest plasma cholesterol than in the highest plasma cholesterol group. Correlation of blood lipid levels with increased risk of cancer occurrence & mortality seemingly make it a pertinent surrogate marker for diagnosis and monitoring in OPMD & OSCC.

The results of the present study show evidence of a significant inverse relationship between the serum lipid profile values in OPMD and OSCC and at least three of the lipid parameters namely TC, HDL and LDL showed significant decrease in both OPMD and OSCC. Variability in other parameters may be attributable to nutritional status, body mass index or even methodological differences.

Conclusions

Hyperlipidemia, has always been a scaring factor for the patients inching towards cardiological ailments. However hypolipidemia in the same tone can also be held as a cause of major serious concerns to the extent of initiating various malignancies including colorectal, breast and also oral cancer. Further such parameters serve as a good indicator and biomarker for many hidden malignancies at their initial or precancerous stages and may give adequate time for their reversals or intervention under appropriate treatment protocol. As per the present study the lower serum lipid status may be considered as a useful indicator for initial changes occurring in the neoplastic cells. The findings of this study suggest that serum lipid profile may be used as a biochemical marker for progression of OPMD and OSCC. Further studies on larger sample size may help to establish Serum Lipid Profile as an adjunct in the mass oral cancer screening programmes and as an aid to early cancer detection.

References

1. Garg D, Sunil MK, Singh PP, Singla N, Rani SA, Kaur B. Serum lipid profile in oral precancer and cancer: a diagnostic or prognostic marker? Journal of international oral health: JIOH. 2014 Apr;6(2):33.

2. Massa no J, Regateiro FS, Januário G, Ferreira A. Oral squamous cell carcinoma: review of prognostic and predictive factors. Oral surgery, oral medicine, oral pathology, oral radiology, and endodontology. 2006 Jul 1;102(1):67-76.

3. Bail wad SA, Singh N, Jani DR, Patil P, Singh M, Deep G, Singh S. Alterations in serum lipid profile patterns in oral cancer: correlation with histological grading and tobacco abuse. Oral Health Dent Manag. 2014 Sep;13(3):573-9.

4. Wang L, Wang X, Li Y, Hou Y, Sun F, Zhou S, Li C, Zhang B. Plasma lipid profiling and diagnostic biomarkers for oral squamous cell carcinoma. Oncotarget. 2017 Nov 3;8(54):92324.

5. Mao L, Hong WK, Papadimitrakopoulou VA. Focus on head and neck cancer. Cancer cell. 2004 Apr 1;5(4):311-6.

6. Le QT, Lee N. Introduction: Head and Neck Cancer. In Seminars in radiation oncology 2012 (Vol. 3, No. 22, pp. 185-186).

7. Niki Takis NG, Pentene Ro M, Georgaki M, Poh CF, Peterson DE, Edwards P, Lingen M, Sauk JJ. Molecular markers associated with development and progression of potentially premalignant oral epithelial lesions: Current knowledge and future implications. Oral surgery, oral medicine, oral pathology and oral radiology. 2018 Jun 1;125(6):650-69.

8. Warnakulasuriya S, Johnson NW, Van der Waal I. Nomenclature and classification of potentially malignant disorders of the oral mucosa. Journal of oral pathology & medicine. 2007 Nov;36(10):575-80.

9. Speight PM, Khurram SA, Kujan O. Oral potentially malignant disorders: risk of progression to malignancy. Oral surgery, oral medicine, oral pathology and oral radiology. 2018 Jun 1;125(6):612-27.

10. Feller L, Lemmer J. Oral squamous cell carcinoma: epidemiology, clinical presentation and treatment.

11. Patil SP, Sodhi SJ, Tam be SD, Gada V, Vik he D. Viruses in Oral Squamous Cell Carcinoma: A Review. Pravara Medical Review. 2016 Mar 1;8(1):4-7.

12. Nayak S, Goel MM, Maker A, Bhatia V, Chandra S, Kumar S, Agarwal SP. Fibroblast growth factor (FGF-2) and its receptors FGFR-2 and FGFR-3 may be putative biomarkers of malignant transformation of potentially malignant oral lesions into oral squamous cell carcinoma. PLoS One. 2015 Oct 14;10(10): e0138801.

13. Sharma N, Khan M. Non-invasive diagnostic tools in early detection of oral epithelial dysplasia.

14. Lohe VK, Degwekar SS, Bhowate RR, Kadu RP, Dan gore SB. Evaluation of correlation of serum lipid profile in patients with oral cancer and precancer and its association with tobacco abuse. Journal of oral pathology & medicine. 2010 Feb;39(2):141-8.

15. Patel PS, Shah MH, Jha FP, Raval GN, Rawal RM, Patel MM, Patel JB, Patel DD. Alterations in plasma lipid profile patterns in head and neck cancer and oral precancerous conditions. Indian journal of cancer. 2004 Jan 1;41(1):25.

16. Odeleye OE, Eskelson CD, Mufti SI, Watson RR. Vitamin E inhibition of lipid peroxidation and Ethanol-mediated promotion of esophageal tumorigenesis.

17. Ajai K, Panat SR, Aggarwal A, Agarwal N, Upadhyay N, Joshi A. Estimation of serum lipids in patients with Oral Submucous Fibrosis in India. Journal of clinical and experimental dentistry. 2014 Jul;6(3): e237.

18. Anne Roth G, Hansen Ls. A methodologic study of histologic classification and grading of malignancy in oral squamous cell carcinoma. European Journal of Oral Sciences. 1984 Oct;92(5):448-68.

19. Bhargava A, Saigal S, Chalishazar M. Histopathological grading systems in oral squamous cell carcinoma: A review. J Int Oral Health. 2010 Dec 1;2(4):1-0.

20. Neerupakam M, Alaparthi RK, Sathish S, Katta SA, Polisetty N, Dam era S. Alterations in plasma lipid profile patterns in oral cancer. Journal of Indian Academy of oral medicine and radiology. 2014 Jul 1;26(3):274.

21. Kumar P, Augustine J, Urs AB, Arora S, Gupta S, Mohanty VR. Serum lipid profile in oral cancer and leukoplakia: correlation with tobacco abuse and histological grading. Journal of cancer research and therapeutics. 2012 Jul 1;8(3):384.

22. Munir R, Usman H, Hasnain S, Smans K, Kalbacher H, Zaidi N. Atypical plasma lipid profile in cancer patients: cause or consequence? Biochimie. 2014 Jul 1; 102:9-18.

23. Beloribi-Djefaflia S, Vasseur S, Guillaumond F. Lipid metabolic reprogramming in cancer cells. Oncogenesis. 2016 Jan;5(1): e189-.

24. Rose G, Shipley MJ. Plasma lipids and mortality: a source of error. The Lancet. 1980 Mar 8;315(8167):523-6.

25. Naik SR, L Ashok, Gupta P. Plasma lip [id profile patterns in oral leukoplakia and oral squamous cell carcinoma. Int. J. of Res. in Pharmacology & Pharmacotherapeutics.2017 Jul;6(3):364-373

26. Chawda JG, Jain SS, Patel HR, Chad uvula N, Patel K. The relationship between serum lipid levels and the risk of oral cancer. Indian journal of medical and

paediatric oncology: official journal of Indian Society of Medical & Paediatric Oncology. 2011 Jan;32(1):34.

27. Singh S, Ramesh V, Premal Atha B, Prasad KV, Rama doss K. Alterations in serum lipid profile patterns in oral cancer. Journal of natural science, biology, and medicine. 2013 Jul;4(2):374.

28. Sherubin EJ, Kannan KS, Kumar DN, Joseph I. Estimation of plasma lipids and its significance on histopathological grades in oral cancer: Prognostic significance original research. Journal of oral and maxillofacial pathology: JOMFP. 2013 Jan;17(1):4.

29. Krontiras H, Roye GD, been ken SE, Myers RB, Mayo MS, Peters GE, Grizzle WE. Fatty acid synthase expression is increased in neoplastic lesions of the oral tongue. Head & Neck: Journal for the Sciences and Specialties of the Head and Neck. 1999 Jul;21(4):325-9.

30. Gupta S, Gupta S. Alterations in serum lipid profile patterns in oral cancer and oral precancerous lesions and conditions—a clinical study. Indian Journal of Dentistry. 2011 Jun 1;2(2):1-7.

31. Mehrotra R, Pandya S, Chaudhary AK, Singh HP, Jaiswal RK, Singh M, Gupta SC, Singh M. Lipid profile in oral submucous fibrosis. Lipids in Health and Disease. 2009 Dec;8(1):1-7.

32. Mehdi pour M, Zenouz AT, Davoodi F, Gholizadeh N, Dam Ghani H, Helli S, Safarnavadeh M. Evaluation of the Relationship between Serum Lipid Profile and Oral Lichen Planus. Journal of dental research, dental clinics, dental prospects. 2015;9(4):261.

33. Swamy KM, Ganiger A. Alterations of serum lipid profile in oral submucous fibrosis. Int J Otorhinolaryngol Head Neck Surg. 2017 Oct; 3:1064.

34. Yashveer JK, Pankaj D. Alteration of Serum Lipid in Oral Sub Mucous Fibrosis in Central India. Indian Journal of Otolaryngology and Head & Neck Surgery. 2018 Sep 1;70(3):421-4.

35. López-Jornet P, Camacho-Alonso F, Rodríguez-Martínes MA. Alterations in serum lipid profile patterns in oral lichen planus. American journal of clinical dermatology. 2012 Dec 1;13(6):399-404.

36. Li G, Da M, Zhang W, Wu H, Ye J, Chen J, Ma L, Gu N, Wu Y, Song X. Alteration of serum lipid profile and its prognostic value in head and neck squamous cell carcinoma. Journal of Oral Pathology & Medicine. 2016 Mar;45(3):167-72.

37. Eichholzer M, Stähelin HB, Gutzwiller F, Lüdin E, Bernasconi F. Association of low plasma cholesterol with mortality for cancer at various sites in men: 17-y follow-up of the prospective Basel study. The American journal of clinical nutrition. 2000 Feb 1;71(2):569-74.

38. Reddy KK, Rao AP, Reddy TP. Serum vitamins E, A and lipid peroxidation levels in Kurichias, an Indian tribal population.