Original Article

Diagnostic significance of serum and salivary lipid levels in oral precancer and oral cancer

ABSTRACT

Introduction: Lipids are one of the major constituents of the cell. Variations in the serum lipids have been considered a cofactor of carcinogenesis, as lipids play a crucial role in cell integrity. Saliva is an ultrafiltrate of plasma and correlates with the serum, which may be used as an alternate method of serum lipid level estimation. The study was conducted to find any correlation between serum and salivary lipid levels and to evaluate the changes in serum and salivary lipid levels in oral precancer and cancer patients. **Aims and Objectives:** This study aimed to evaluate the changes in serum and salivary lipid levels in oral precancer and cancer patients and to correlate salivary lipid levels with serum lipid levels. **Materials and Methods:** The study was an *in vivo* study conducted on randomly selected 129 patients with oral cancer and oral precancer. The selected subjects were divided into four groups as Group 1 – healthy control, Group 2 – oral submucous fibrosis, Group 3 – leukoplakia, and Group 4 – oral cancer. Serum and salivary lipid levels were estimated biochemically and statistically analyzed for any correlation with oral precancer and cancer. **Results:** Lipid level estimation showed no statistically significant difference on comparison of intergroup serum and saliva total cholesterol level and high-density lipoproteins among all four groups, whereas intergroup comparison of serum and saliva triglycerides (TG) levels among the four groups showed a statistically significant difference in saliva TG level. The correlation of serum and salivary lipid levels showed a significant positive correlation. **Conclusion:** In the present study association between serum/salivary lipid levels and oral precancer and oral cancer could not be established. A positive association was there in serum and salivary lipids hence salivary lipid levels may be used as a noninvasive technique for serum lipid level estimation.

Keywords: Oral cancer, oral precancer, salivary cholesterol, salivary high-density lipoproteins, salivary low-density lipoproteins, salivary lipids, serum lipids

INTRODUCTION

Lipids are one of the major constituents of cells; they include triglycerides (TG), total cholesterol, low-density lipoproteins (LDL), high-density lipoproteins (HDL), very LDL, and chylomicrons. Variations in the serum lipid parameters have been considered as one of the cofactors of carcinogenesis. Lipids play a key role in various biological functions such as stabilization of DNA helix, cell growth, and maintenance in normal as well as in malignant tissues.[1] There are evidences of significant changes usually lowering of the serum lipid levels during malignant transformation; these lowered levels in serum could be due to the course of carcinogenesis.[2] There are conflicting hypotheses regarding hypolipidemia and carcinogenesis. According to few theories, carcinogenesis results in hypolipidemia. The increased requirement of the lipids for the growth of the malignant cells leads to depletion of the lipid stores. Other theories believe that there is a generation of free radicals,

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responsible for oxidation/peroxidation of lipids leading to cell membrane defect and carcinogenesis.[3] Based on these theories serum lipid levels could be used as a marker of malignant transformation. Saliva is an ultrafiltrate of plasma and correlates with the serum, which may be used as an alternate method of serum lipid level estimation.[4] Moreover, nearly 40% of the proteins that are responsible for various diseases such as cancer, cardiovascular disease, and stroke may be found in the whole saliva.[5] Saliva is used and well authenticated in identifying, monitoring, and predicting disease progression in the upcoming diagnostic era; hence, in future diagnostic strategies, saliva can provide an effective noninvasive approach for screening oral precancer and cancer for a large population in the community.

Considering the above facts about the importance of serum and salivary lipid levels as a diagnostic marker of precancer and cancer, the study was designed to evaluate the changes in serum and salivary lipid levels in oral precancer and cancer patients and to correlate serum lipids with salivary lipid levels.

MATERIALS AND METHODS

The study was an *in vivo* study conducted with institutional ethical approval (ref no. 3786/ethical/R.Cell-15 dated March 3, 2015). One hundred and twenty-nine patients were randomly selected after informed consent from the outpatient department of the institution.

Individuals with clinical evidence and histopathologically confirmed oral precancer and cancer were included in the study. The selected subjects were divided into four groups as Group 1 – healthy control, Group 2 – oral submucous fibrosis (OSMF), Group 3 – leukoplakia, and Group 4 – oral cancer. Subjects having known systemic or skin diseases and who have undergone previous radiotherapy, surgery, or chemotherapy were excluded. In fasting condition, 2 ml of blood was withdrawn from the antecubital vein of the subjects. The serum was separated by centrifugation at 40°C and the supernatant was analyzed. About 1 ml of unstimulated whole saliva was collected in restful and fasting conditions for 5 min by the subjects leaning forward and spitting saliva into test tubes and these samples were analyzed for lipid levels. Total cholesterol, HDL, and triglyceride levels were estimated using Q-Line S+· Selectra system reagents. Serum/salivary total cholesterol was analyzed by enzymatic CHOD-PAP method, endpoint using a cholesterol reagent. HDL was analyzed by direct rnzymatic (polyvinyl sulfonic acid/polyethylene-glycol ether) method, endpoint using a precipitating reagent, and triglyceride levels by enzymatic (GPO-PAP) calorimetric method, endpoint using a triglyceride reagent. The absorbance of standard test against blank was read at 506/630 nm using a biochemistry autoanalyzer.

Statistical analysis
Evaluation of results and statistical analysis was done using one-way analysis of variance and correlation-regression analysis.

RESULTS

One hundred and twenty-nine subjects were included in the study on the basis of the inclusion and exclusion criteria with a mean age of 43 years. Among the study subjects, 25 (19.4%) healthy control, 26 (20.2%) OSMF cases, 26 (20.2%) leukoplakia, and 52 (40.3%) were oral cancer cases [Table 1].

The age groups of 18–25 years, 26–35 years, 36–45 years and >45 years were in the proportion of 14%, 20.2%, 27.9%, and 38.0% in the study, respectively. The male-to-female ratio in the study was 66.7%:33.3% [Table 2].

Lipid level estimation showed no statistically significant difference in serum and saliva total cholesterol [Table 3] and HDL levels [Table 4] among all the four groups. Whereas intergroup comparison of serum and Saliva TG Level among the four groups showed a statistically significant difference in saliva TG level, the minimum level was observed in healthy control while maximum in leukoplakia ($P = 0.041$) [Table 5].

Correlation of serum and salivary total cholesterol level [Table 6], triglyceride levels [Table 7], and HDL levels [Table 8] showed a significant positive correlation. The degree of correlation was varied in different groups. The correlation between salivary cholesterol level and serum cholesterol level was moderately positive for overall ($r = 0.437$, $P < 0.001$), strongly positive for healthy control ($r = 0.560$, $P = 0.004$), OSMF ($r = 0.527$, $P = 0.006$), and leukoplakia ($r = 0.625$, $P = 0.001$) but was weakly positive for oral Cancer ($r = 0.304$, $P = 0.029$). The correlation between salivary triglyceride level with serum triglyceride level was strongly positive for

Table 1: Age distribution of cases among the groups

Group	Total, *n* (%)
Healthy control	25 (19.4)
OSMF	26 (20.2)
Leukoplakia	26 (20.2)
Oral cancer	52 (40.3)

OSMF: Oral submucous fibrosis

Table 2: Distribution of cases according to age and gender

Variable	Diagnosis				Total, *n* (%)
	Healthy control, *n* (%)	OSMF, *n* (%)	Leukoplakia, *n* (%)	Oral cancer, *n* (%)	
Age (year)					
18-25	10 (55.6)	5 (27.8)	2 (11.1)	1 (5.6)	18 (14.0)
26-35	9 (34.6)	8 (30.8)	2 (7.7)	7 (26.9)	26 (20.2)
36-45	5 (13.9)	9 (25.0)	8 (22.2)	14 (38.9)	36 (27.9)
>45	1 (2.0)	4 (8.2)	14 (28.6)	30 (61.2)	49 (38.0)
Gender					
Female	11 (25.6)	7 (16.3)	7 (16.3)	18 (41.9)	43 (33.3)
Male	14 (16.3)	19 (22.1)	19 (22.1)	34 (39.5)	86 (66.7)
Total	25 (19.4)	26 (20.2)	26 (20.2)	52 (40.3)	129 (100.0)

OSMF: Oral submucous fibrosis

Table 3: Intergroup comparison of serum and saliva cholesterol level

Parameter	Group	Mean	SD	Minimum	Maximum	F	P
Serum cholesterol	Healthy control	154.32	30.41	91.40	206.00	2.03	0.113
	OSMF	181.37	51.08	91.40	282.00		
	Leukoplakia	177.90	38.53	125.30	251.70		
	Oral cancer	178.29	50.66	16.51	258.50		
Saliva cholesterol	Healthy control	7.66	3.97	3.10	16.80	1.35	0.261
	OSMF	26.20	63.99	1.00	328.80		
	Leukoplakia	22.90	35.17	3.10	157.60		
	Oral cancer	26.43	37.31	1.50	139.47		

SD: Standard deviation, OSMF: Oral submucous fibrosis

Table 4: Intergroup comparison of serum and saliva high density lipoproteins level

Parameter	Group	Mean	SD	Minimum	Maximum	F	P
Serum HDL	Healthy control	43.81	8.21	25.70	58.60	2.19	0.093
	OSMF	52.00	18.81	27.70	91.60		
	Leukoplakia	44.44	7.05	27.50	55.20		
	Oral cancer	46.39	13.15	3.00	72.80		
Saliva HDL	Healthy control	3.41	2.77	0.40	8.80	0.39	0.761
	OSMF	3.41	5.45	0.60	25.60		
	Leukoplakia	2.78	6.92	0.10	36.30		
	Oral cancer	4.28	7.04	0.60	48.70		

SD: Standard deviation, OSMF: Oral submucous fibrosis, HDL: High-density lipoproteins

Table 5: Intergroup comparison of serum and saliva triglycerides level

Parameter	Group	Mean	SD	Minimum	Maximum	F	P
Serum TG	Healthy control	139.25	75.34	60.60	327.80	0.90	0.442
	OSMF	175.76	134.33	37.00	719.50		
	Leukoplakia	201.06	198.43	40.20	801.70		
	Oral cancer	166.46	120.91	10.40	773.00		
Saliva TG	Healthy control	5.98	3.82	2.00	16.40	2.84	0.041
	OSMF	29.80	51.52	0.70	206.00		
	Leukoplakia	45.16	61.71	0.50	207.40		
	Oral cancer	29.61	50.77	0.70	218.70		

SD: Standard deviation, OSMF: Oral submucous fibrosis, TG: Triglyceride

overall cases ($r = 0.617$, $P < 0.001$), OSMF ($r = 0.720$, $P < 0.001$), leukoplakia ($r = 0.664$, $P < 0.001$) but was moderately positive in oral Cancer ($r = 0.543$, $P < 0.001$) and healthy control ($r = 0.507$, $P = 0.010$). On comparing saliva HDL level with serum HDL level, there was a weak correlation in overall cases ($r = 0.406$, $P < 0.001$) and oral Cancer ($r = 0.377$, $P = 0.006$), moderate correlation in healthy control ($r = 0.516$, $P = 0.008$), strong correlation in OSMF ($r = 0.628$, $P = 0.001$) but insignificant in leukoplakia ($r = 0.322$, $P = 0.109$).

Table 6: Correlation of serum cholesterol level with saliva cholesterol level

Cholesterol	Saliva versus serum	
	Pearson correlation	P
Overall	0.437	<0.001
Healthy control	0.560	0.004
OSMF	0.527	0.006
Leukoplakia	0.625	0.001
Oral cancer	0.304	0.029

OSMF: Oral submucous fibrosis

Table 7: Correlation of serum triglyceride level with saliva triglyceride level

TGs	Saliva versus serum	
	Pearson correlation	P
Overall	0.617	<0.001
Healthy control	0.507	0.010
OSMF	0.720	<0.001
Leukoplakia	0.664	<0.001
Oral cancer	0.543	<0.001

TGs: Triglycerides, OSMF: Oral submucous fibrosis

Table 8: Correlation of serum high-density lipoproteins level with saliva high-density lipoproteins level

HDL	Saliva vesus serum	
	Pearson correlation	P
Overall	0.406	<0.001
Healthy control	0.516	0.008
OSMF	0.628	0.001
Leukoplakia	0.322	0.109
Oral cancer	0.377	0.006

HDL: High-density lipoproteins, OSMF: Oral submucous fibrosis

DISCUSSION

Oral cancer is the sixth most common cancer in the world.[6] Oral potentially malignant disorders may transform into cancer of the oral cavity, early diagnosis of these lesions and oral cancer as well may lead to better control and prevention. Continuously various biomarkers are being searched to diagnose the oral precancer and oral cancer at the initial stage. Serum lipid levels play a pivotal role in the cell wall integrity, whereas dyslipidemia may result in cell wall transformation or carcinogenesis. Many types of cancers have been associated with altered levels of plasma lipids, particularly HDL and TG.[7] Estimation of serum lipid levels could be an excellent diagnostic means to detect the initiation of oral precancer and cancer.[8]

The present study was conducted on 129 subjects of mean age 43 years with the highest number of patients above 36 years of age. It is well-documented that the incidence of oral cancer increases with age.[9]

The selected sample showed male predominance which could be attributed to the fact the tobacco chewing and smoking habit is more common in males.[10]

It has been seen that there is a reduction in plasma lipid levels during the development of neoplasia but not prior to its beginning. Various studies provide evidence for an increased uptake of lipids by tumor cells and for its role in carcinogenesis. Rose and Shipley reported an inverse association between serum lipid levels and the risk of cancer.[11] In our study, we could not find a statistically significant difference in serum and salivary lipid levels among the various study groups. The present study does not account any significant association between lipid levels and oral precancer and oral cancer.

Saliva is an ultrafiltrate of blood, it contains most of the constitutes of serum and may be used as an alternate of serum. As a clinical marker, saliva has some extra advantages over serum. In parts of patients, this is a noninvasive sampling technique, greatly reduces apprehension and discomfort and supports repeated sampling.[12] Handling of saliva is easier for diagnostic procedures as no chance of clotting, and analysis of saliva may provide a cost-effective method for the mass screening.

The present study was also designed to analyze the role of saliva as an alternate of serum. In our study, there was a significant moderate positive correlation between serum and salivary lipid levels in all the study groups. Singh *et al*. found moderate positive correlation between saliva and serum lipid levels, whereas Kale *et al*. reported a strong positive correlation between saliva and serum lipid levels. Karjalainen *et al*. also observed weak positive correlations between saliva and serum cholesterol levels and saliva and serum non-HDL cholesterol concentrations.[13-15] The present study reveals that the salivary lipid levels may be used as an indicator of serum lipid levels and used as noninvasive technique for serum lipid level estimation.

The study was conducted on the subjects of limited geographic distribution and other cofactors such as harmful habits such as alcohol, smoking, body mass index, and dietary habits were not reckoned so these could be considered as drawbacks of our study.

Although in the present study any association between serum and salivary lipid levels and oral precancer and oral cancer could not be established, we could accomplish more multicentric studies with a larger number of subjects to establish the possible role of serum or salivary lipid levels in the process of oral precancer and cancer.

CONCLUSION

From the present study, we can assume that salivary lipids can be used as an alternative noninvasive method of serum lipid level estimation, as serum and salivary lipid levels showed a good positive correlation. However, the role of lipid levels in oral precancer and cancer yet to be established. We need further multicentric studies with a large sample size and associated cofactors to explore the probable role of lipid levels in the development of oral-precancer and cancer.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Mehta R, Gurudath S, Dayansoor S, Pai A, Ganapathy KS. Serum lipid profile in patients with oral cancer and oral precancerous conditions. Dent Res J (Isfahan) 2014;11:345-50.
2. Subbulakshmi AC, Mohan N, Thiruneervannan R, Naveen S. Comparative evaluation of serum lipid profile in patients with oral submucous fibrosis and oral squamous cell carcinoma with that of control subjects: A case control study. J Pharm Bioallied Sci 2017;9:S191-6.
3. Chawda JG, Jain SS, Patel HR, Chaduvula N, Patel K. The relationship between serum lipid levels and the risk of oral cancer. Indian J Med Paediatr Oncol 2011;32:34-7.
4. AL-Rawi N, Atiyah K. Assessment of Salivary lipid profiles in patients with ischemic stroke and patients at risk of having stroke among Iraqi sample. Internet J Third World Med 2007;1:1-9.
5. Loo JA, Yan W, Ramachandran P, Wong DT. Comparative human salivary and plasma proteomes. J Dent Res 2010;89:1016-23.
6. Borse V, Konwar AN, Buragohain P. Oral cancer diagnosis and perspectives in India. Sens Int 2020;1:100046.
7. Pandeya DR, Rajbhandari A, Nepal M, Abdalhabib EK, Bhatta M, Malla SS, *et al*. Comparative study of serum lipid profiles in nepalese cancer patients attending a tertiary care hospital. Asian Pac J Cancer Prev 2018;19:491-5.
8. 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. J Cancer Res Ther 2012;8:384-8.
9. Rocha TA, Thomaz EB, da Silva NC, de Sousa Queiroz RC, de Souza MR, Barbosa AC, *et al*. Oral primary care: An analysis of its impact on the incidence and mortality rates of oral cancer. BMC Cancer 2017;17:706.
10. Singh A, Ladusingh L. Prevalence and determinants of tobacco use in India: Evidence from recent Global Adult Tobacco Survey data. PLoS One 2014;9:e114073.
11. Rose G, Shipley MJ. Plasma lipids and mortality: A source of error. Lancet 1980;1:523-6.
12. Javaid MA, Ahmed AS, Durand R, Tran SD. Saliva as a diagnostic tool for oral and systemic diseases. J Oral Biol Craniofac Res 2016;6:66-75.
13. Singh S, Ramesh V, Oza N, Balamurali PD, Prashad KV, Balakrishnan P. Evaluation of serum and salivary lipid profile: A correlative study. J Oral Maxillofac Pathol 2014;18:4-8.
14. Karjalainen S, Sewón L, Söderling E, Larsson B, Johansson I, Simell O, *et al*. Salivary cholesterol of healthy adults in relation to serum cholesterol concentration and oral health. J Dent Res 1997;76:1637-43.
15. Kale K, Iyengar A, Kapila R, Chhabra V. Saliva – A diagnostic tool in assessment of lipid profile. Sch Acad J Biosci 2017;5:574-84.